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THE MICROSCOPICAL AND CHEMICAL EXAMINATION OF COMMERCIAL GINGER.*

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Besides its use in medicine, ginger is extensively used in the United States, both as a condiment and confection, and also in the preparation of ginger ale. While there are about twenty species of the genus *Zingiber*, most of the commercial article is obtained from *Zingiber officinale*, Roscoe. According to Watt,[1] this species is not known in a truly wild state, but is doubtless a native of Tropical Asia. It is now extensively cultivated in both the Eastern and Western Hemispheres, having been introduced into nearly all tropical countries.

It is a perennial herbaceous plant, belonging to the family *Zingiberaceæ*, a monocotyledonous group of plants which are characterized by their aromatic properties. The plant produces two kinds of shoots, one composed of leaves only and one which bears flowers. It is of interest to note in this connection that although the plant is grown in many of the botanic gardens of the world, it is claimed by Bentley and Trimen[2] that it does not flower under these conditions. An excellent illustration of the plant is given by Berg and Schmidt,[3] and this has been reproduced by Engler and Prantl[4] and other authors.

* This is the second of this series of papers, the first having appeared in the January number of this Journal on the "Examination of Black Pepper." It probably should be stated that the chemical analyses given in this series of papers are being carried on by Mr. Sindall, the remaining part of the work being by Professor Kraemer.

When grown for commercial purposes, the plant is propagated from cuttings of the rhizomes. In India great care is bestowed upon this crop, special attention being given both to the physical condition of the soil and its composition. Frequently the *Dolichos* vine is grown along with the ginger plants to keep the ground moist and cool, or the plants are protected by a leafy covering. The cuttings are planted in April or May, or later, according to locality, and it takes about nine months for the plant to reach maturity. In Jamaica the planting season begins in March or April.

When the overground parts of the plants die down, the rhizomes are dug and variously treated to prepare them for market. In Jamaica, according to Kilmer,[5] the rhizomes are first peeled and then washed with clean water, in some cases lime-juice being added to the water, after which they are dried in the sun. In India the rhizomes are usually partly peeled and treated with boiling water, or, according to Simmonds,[6] with boiling lime water. In some cases the peeled rhizomes are subsequently coated with calcium carbonate (chalk) or calcium sulphate (gypsum) to prevent the ravages of insects. Decorticated ginger is often bleached by the use of chlorinated lime or sulphurous acid.

The rhizome is described as being a sympodium, that is, belongs to the dichotomous system of branching, in which the branches on one side are less developed. Its external morphology, as well as histology, has been studied by Meyer,[7] and by Oesterle and Tschirch.[8] The rhizome is flattened, and as a result of its branching habit assumes the peculiar form sometimes spoken of as a "hand," the branches being called "fingers."

DESCRIPTION OF COMMERCIAL GINGERS.

Gingers are known commercially as "scraped" or "decorticated," and "coated," the scraped including those sorts from which the cortex has been removed in whole or in part by peeling, as the Cochin, Jamaica and Japan gingers; whereas the coated gingers include those which retain the periderm or outer natural layers of the rhizomes, as African, Calcutta and Calicut. "Bleached" and "unbleached" sorts are also distinguished, the former including rhizomes which are lighter in color, owing to careful washing and drying or other treatment as already stated. There has long been a demand for "white ginger," which demand has been met by coat-

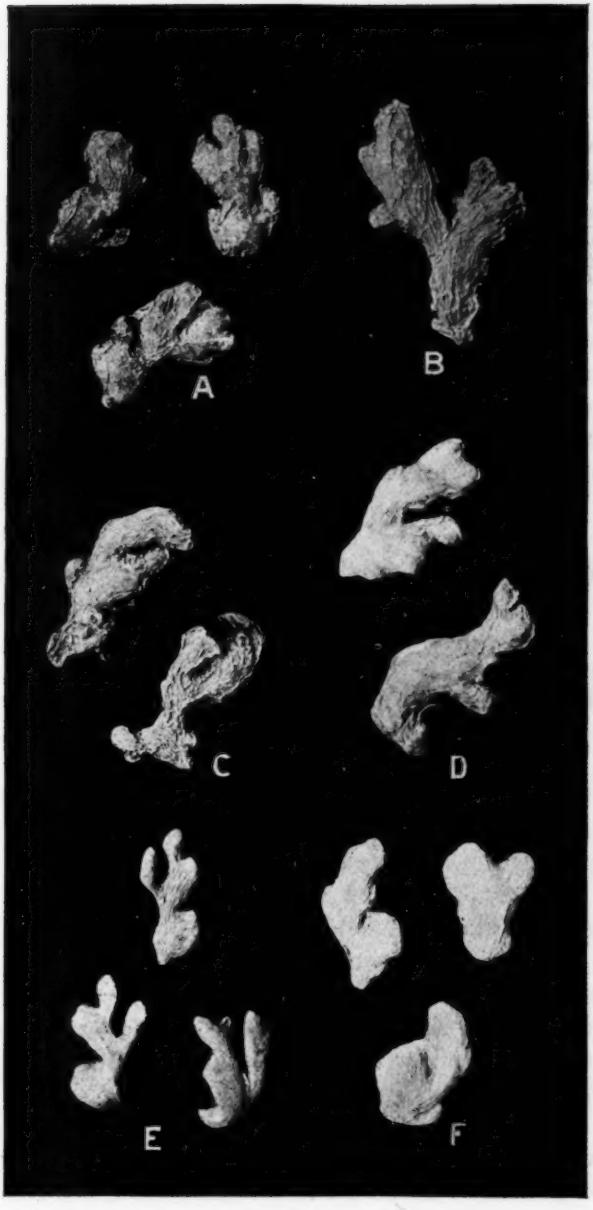

FIG. 1.—Commercial gingers: *A*, African; *B*, Calcutta; *C*, Calicut; *D*, Cochin; *E*, Jamaica; *F*, Japan. (One half natural size).

ing the rhizomes with lime. The United States Government standards do not, however, permit any considerable percentage of lime, but, on the contrary, require the gingers of the market to be carefully garbled, and that only clean pieces be used.

The principal commercial gingers which are coming into this market at present are African, Calcutta, Calicut, Cochin, Jamaica and Japan (*Fig. 1*).

African Ginger.—This sort occurs in short-branched pieces (*Fig. 1*) that vary from 2 to 4 cm. in length, and from 6 to 12 mm. in width. The pieces are partly peeled on the flattened sides, the patches where the cortex is removed being smooth and of a brown color. The unpeeled portion is longitudinally wrinkled, or reticulate, and of a grayish-brown color. The fracture is short or short-fibrous. Internally, the color varies from lemon-yellow to a dark-bluish or slate color, and the sections exhibit yellowish oil dots and light-yellow to garnet resin dots. The odor is strongly aromatic and the taste is intensely acrid.

Calcutta Ginger.—This ginger somewhat resembles the African ginger, but the branches or fingers are larger, and there is a considerable proportion of shriveled pieces. The pieces vary from 2 to 7 cm. long, and from 5 to 20 mm. wide. The color is grayish-brown, the peeled parts being of a grayish-blue or slate color, due to the presence of a mold. The fracture is short and mealy, or horny. Internally, the rhizome is of a light yellow or light brownish-yellow color, and exhibits resin dots which are yellow to yellowish-brown in color. The odor is aromatic, and the taste starchy and strongly pungent.

Calicut Ginger.—The pieces of this sort resemble those of Calcutta ginger, but more of the periderm is removed. They are from 2·5 to 5·5 cm. long and from 10 to 18 mm. wide. The color is more or less uniformly light brown. The fracture is short, or short-fibrous, and mealy. The color internally is light or brownish-yellow, the resin dots under the lens being yellowish. The odor is aromatic and the taste is strongly acrid.

Cochin Ginger.—The pieces are more or less plump and uniform in size, varying from 2 to 4 cm. long, and from 10 to 20 mm. wide. A large proportion of the periderm is removed, and the color varies from a light brown to a grayish-yellow. The fracture is short and mealy. Internally, the pieces are of a light cream color, and under

a lens show numerous black resin dots. The odor is aromatic and the taste is acrid, but less persistent than in some of the other kinds.

Jamaica Ginger.—The main branches of the rhizome appear to

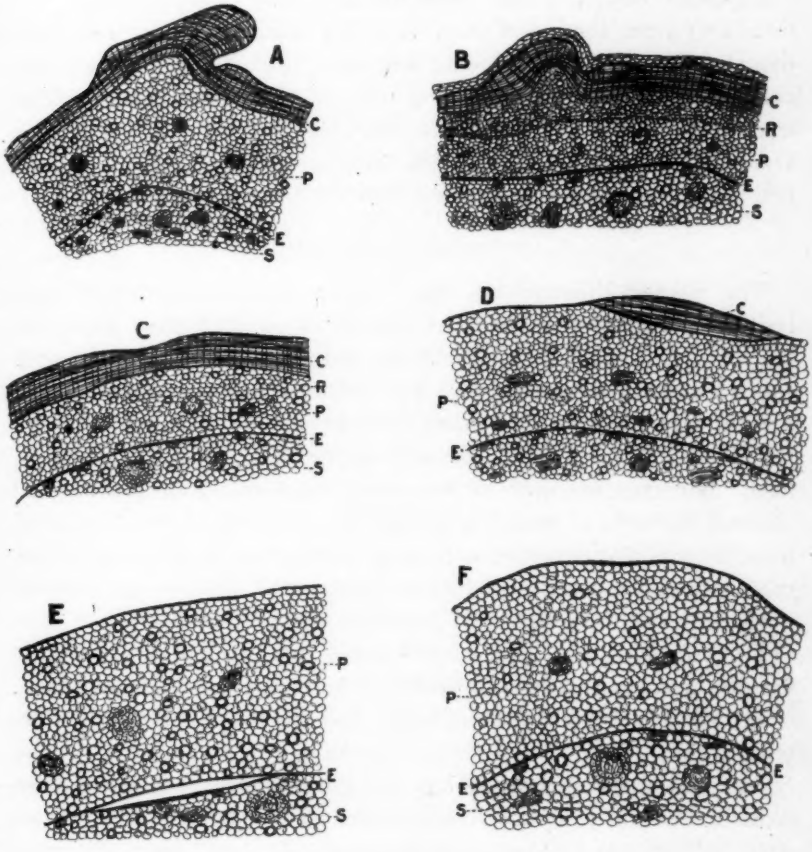

FIG. 2.—Transverse sections showing relative width of cortex in the following commercial gingers: *A*, African; *B*, Calcutta; *C*, Calicut; *D*, Cochin; *E*, Jamaica; *F*, Japan.

C, cork; R, pigment layer; P, parenchyma of cortex, containing secretion cells and fibrovascular bundles; E, endodermis; S, stele with parenchyma, secretion cells and fibrovascular bundles.

be comparatively small, and the pieces vary from 2 to 4 cm. long, and from 2 to 17 mm. wide. All of the periderm is removed and the surface is smooth and grayish-white to dark gray in color. The

fracture is short and smooth. The color internally is light yellowish-brown, showing few reddish-yellow resin dots under a lens. The odor is very aromatic and the taste agreeably pungent.

Japanese Ginger.—The pieces are sparingly branched and vary from 2 to 4 cm. long, and from 10 to 20 mm. in width. The periderm is mostly removed, the surface being smooth and of a whitish color, due to the presence of a coating of calcium carbonate. The fracture is short and very mealy, the color internally varying from cream to light brown. Under the lens the sections exhibit reddish resin dots. The odor is aromatic and the taste is acrid.

MICROSCOPIC STRUCTURE.

The ginger rhizome has the typical monocotyledonous stem structure (*Fig. 2*). It consists chiefly of parenchyma containing starch, among the cells of which are numerous secretion cells with suberized walls that contain oil and resinous substances, and about one-third to one-fourth as many fibrovascular bundles, which are of the closed collateral type. Separating the central cylinder, or stele, from the cortex, is a more or less interrupted endodermis, the radial walls of the cells of which are slightly suberized, but in the dried material it is distinguished with some difficulty. A portion of the cork is found in African, Calcutta, Calicut and Cochin gingers, but is wanting in the Jamaica and Japan varieties.

Parenchyma.—The parenchyma cells are nearly isodiametric, varying from 25 to 120 μ in diameter, and are somewhat elongated. The walls are composed of cellulose and are about 1 μ thick. The parenchyma cells of the stele are uniformly larger than those of the cortex. It has been stated that the parenchyma contains calcium oxalate, but this substance has not been detected in the commercial sorts included in this examination, the cells containing starch as already stated.

Starch Grains.—The careful study of the starch grains of ginger is very important, for not only may the different commercial sorts be distinguished by the characters of the starch grains, but their appearance also possibly throws some light on the manner of curing of the rhizomes. While it is true that the starch grains vary considerably in the same ginger as well as in the different gingers, still they possess some dominant characters which serve to distinguish to a certain extent the different commercial gingers. In a general

way the grains vary from irregular-spherical to ellipsoidal, ovoid, ovoid-pointed and somewhat rectangular as viewed on the side (*Fig. 3*). While occasionally a grain may show distinct lamellæ, this is not the rule. For some reason ginger starch grains do not polarize well. Very few of the grains show a distinct cross, and usually the contrast in the parts of the field is faint, unless they are mounted in oil and heated to 60° C.

The starch grains of Japan ginger are the most easily distinguished. In addition to the typical grains, which vary from 20 to 35 μ in length, there are numerous compound grains varying from 4 to 25 μ in diameter (*Fig. 3, f*). They differ from the ordinary compound grains by being more or less irregular and of varying size, and apparently more easily detached from one another than is usually the case. In Calcutta ginger there appears to be a larger proportion of spherical grains, reminding one of those of wheat, and varying from 15 to 25 μ in diameter. The larger grains are ovoid, pear-shaped, or ovoid and beaked, and not more than 30 to 40 μ in diameter (*Fig. 3, b*). In Jamaica ginger the grains are uniformly larger than in the other gingers, it being not unusual to find them 45 μ long and occasionally 60 μ long (*Fig. 3, e*). The starch grains of African, Calicut and Cochin gingers are quite similar, and vary in diameter from 20 to 45 μ. In Calicut ginger there are, however, a few compound grains and a considerable number of helmet-shaped grains (*Fig. 3, c*). In Cochin ginger the grains show a stronger polarization than those of the other gingers, even when mounted in water (*Fig. 3, d*). In African ginger there is a preponderance of ellipsoidal, ovoid and pear-shaped grains, which on an average are from 25 to 30 μ in length (*Fig. 3, a*).

Secretion Cells.—In ginger there are two kinds of secretion cells, one kind being found with the parenchyma and being nearly spherical, and another associated with the fibrovascular bundles and elongated. Those found in the parenchyma vary in number from 10 to 50 per square millimeter as viewed in transverse section, and are more numerous in the cortex than in the stele, and furthermore occur in greater number near the endodermis (*Fig. 2*). The cells vary in diameter from 45 to 150 μ. The largest of these cells are found in Japan ginger. In fresh ginger and in the confection known as "crystallized ginger," the contents are oily and of a light yellow color, changing to a golden yellow with sulphuric acid. In most of

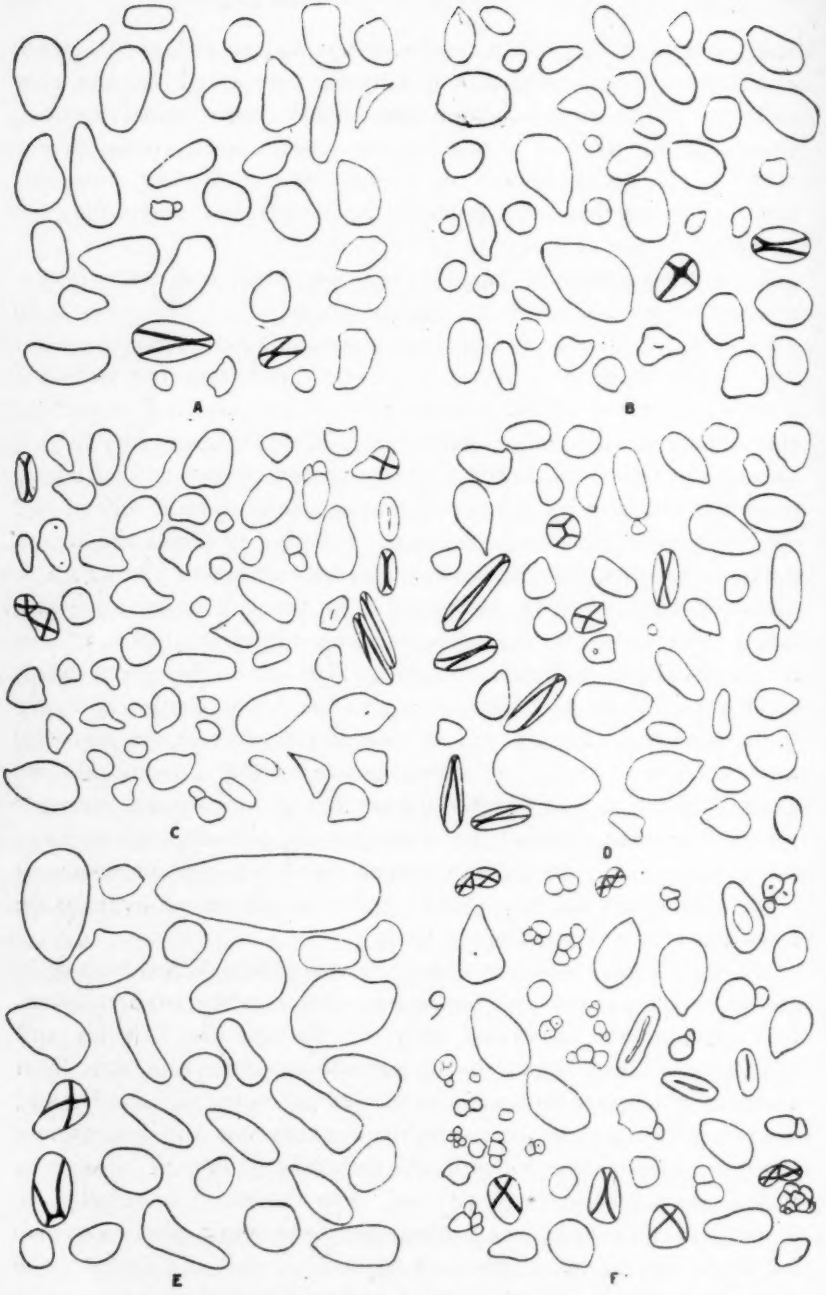

FIG. 3.—Starch grains of the following commercial gingers: *A*, African; *B*, Calcutta; *C*, Calicut; *D*, Cochin; *E*, Jamaica; *F*, Japan.

the dried commercial specimens the contents consist of a yellowish to reddish-brown balsam-like or resinous substance, which becomes of a deep brownish-black color on treatment with sulphuric acid. In Cochin ginger many of these cells contain a black tar-like product.

The elongated secretion cells are from 60 to 150 μ long and from 9 to 15 μ in diameter. They are somewhat irregular in outline and more or less pointed at the ends. In dried material the contents are of a yellow or bright yellowish-brown color.

Fibrovascular Bundles.—The fibrovascular bundles are, as already stated, of the closed collateral type, and the group of cells composing them vary in diameter from 60 to 360 μ, the smaller bundles always being in the region of the endodermis, and the larger occurring in the stele, and averaging from three to five in number per square millimeter. The bundles may consist entirely of two or three tracheæ and accompanying sieve cells, or they may include, in addition, from two or three to forty-five or fifty sclerenchymatous fibers. The latter appear to be more numerous in the Calcutta and Calicut gingers. The tracheæ are mostly reticulate, and vary from 30 to 60 μ in diameter (*Fig. 5*). The walls consist mostly of cellulose and contain little or no lignin, that is, the reaction with phloroglucin is very obscure. The sclerenchymatous fibers vary from 0·3 to 1·3 mm. long, and from 20 to 30 μ in diameter. The walls are about 3 μ thick, slightly yellowish, and have slender oblique simple pores. The walls are said to be slightly lignified, but this does not appear to be true of the samples herein described. They readily swell with sulphuric acid, are first colored deeper yellow with chlor-zinc-iodide, then blue, and are not affected by phloroglucin and hydrochloric acid. The fibers are easily separated either in the crude drug or powder by the use of Schulze's macerating fluid, and some of the more typical ones from the different gingers are shown in Fig. 4.

Endodermis.—The endodermal cells are not especially characteristic, but on treatment with sulphuric acid the radial walls are seen to be suberized. Sometimes the other walls appear to be partly suberized. The cells are from 60 to 90 μ long and about 12 μ in diameter.

Cork.—The cork cells are of the usual type, and in the African ginger the cork layer is about 0·3 mm. thick; in Calcutta ginger, about 0·4 mm. thick. The cells are on an average about 60 μ long, and 25 μ wide.

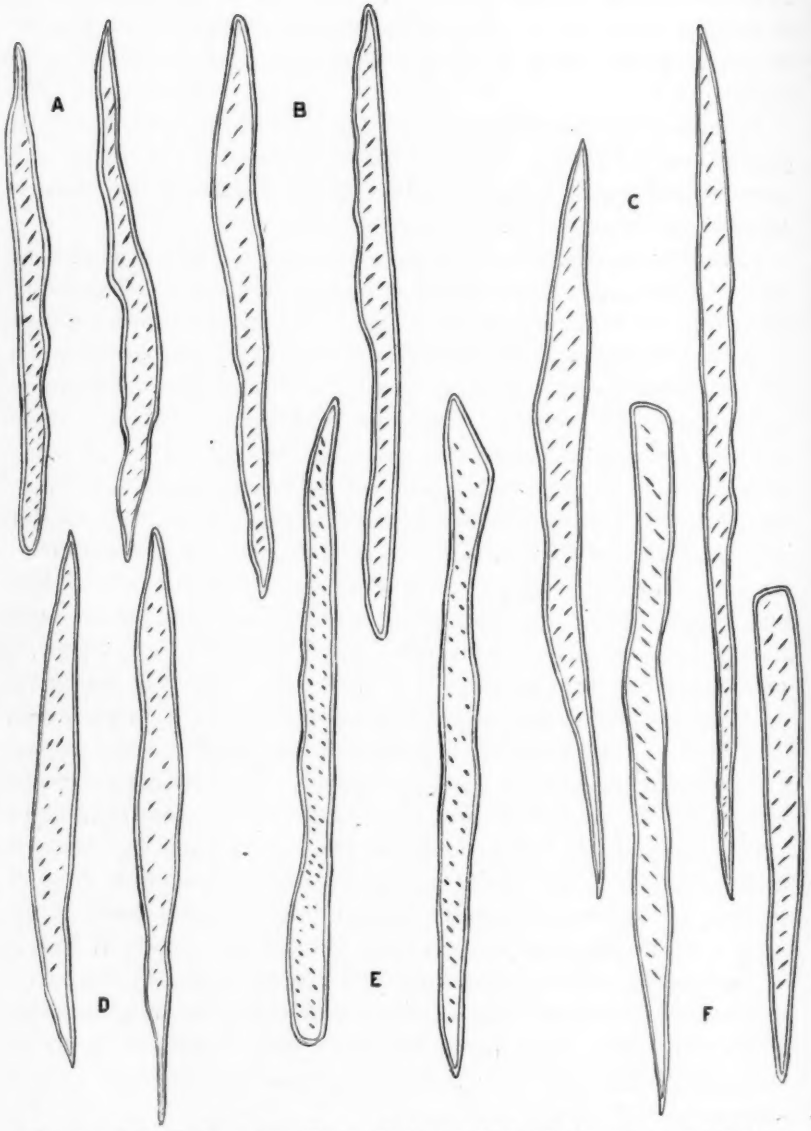

FIG. 4.—Sclerenchymatous fibers of gingers isolated by means of Schulze's macerating fluid: *A*, African; *B*, Calcutta; *C*, Calicut; *D*, Cochin; *E*, Jamaica; *F*, Japan.

Ground or Powdered Ginger.—The color of powdered ginger varies from pale yellow to light or dark brown. The odor is strongly aromatic and characteristic, and the taste is very pungent. In the making of the tincture of ginger, the U. S. Pharmacopœia directs that the ginger shall be in the form of a moderately fine powder, that is, the particles composing the powder shall be about 0·5 mm. in diameter. An examination of the commercial powdered ginger shows that the particles exclusive of starch grains vary from 0·1 to 0·6 mm. in diameter. Buchwald[9] call attention to the fact that when powdered ginger is dropped upon the surface of water the particles rapidly separate from one another and then sink in the liquid. This behavior of the ginger particles is all the more marked when it is compared with that of ether-extracted ginger, starch or lycopodium. When powdered ginger is treated with pure sulphuric acid, a reddish-brown color is at first produced, which rapidly changes to dark brown and finally to purplish-brown.

In the microscopic examination of the powders (*Fig. 5*) it is necessary to use several reagents. After making a preliminary examination of the material mounted in water, portions of the powders may then be mounted in one of the fixed oils, as olive or almond. While this medium brings out all of the elements of the powder, it is especially useful in the study of the starch grains. For this purpose it is necessary to use a small quantity of material, not more than a milligram to two or three drops of oil. The entire field should be examined carefully and the size and shape of the grains noted. If the preparation be heated at a temperature of 60° C. for 10 to 15 minutes, the polarizing effects of the grains become more pronounced (*Fig. 3*). Inasmuch as there are no lignified cells in ginger, phloroglucin is another important reagent in the examination of the powder, serving to detect any of the usual adulterants which contain lignified cells, as wheat middlings or capsicum. The sclerenchymatous fibers may be isolated by the use of Schulze's macerating fluid. When the cells are separated, the material is mounted in alcoholic methylene blue and glycerin is added (*Fig. 4*). Sulphuric acid is not only useful for determining the presence of ether-exhausted ginger and distinguishing the oil and resin cells, and the presence or absence of cork, but is especially useful in detecting the fungus of moldy ginger, the hyphæ and spores being both brought out with this reagent.

Adulterated Ginger.—The study of ginger is rendered difficult by reason of the fact that in preparing it for the market it is treated in a manner which alters its character to a greater or lesser extent.

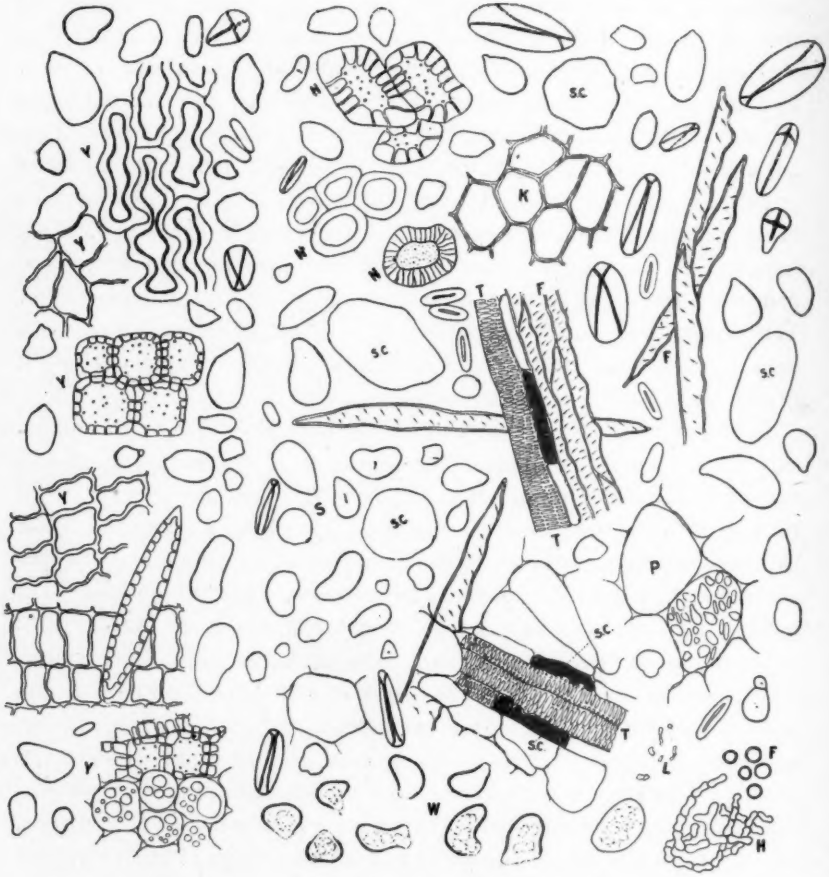

FIG. 5.—Adulterated powdered ginger: F, sclerenchymatous fibers; T, reticulate tracheæ; SC, secretion cells; K, cork; S, starch grains; W, swollen starch grains; W, small swollen altered starch grains; P, parenchyma; H, hyphæ of fungus and spores (F); Y, fragments of tissues of capsicum; N, stone cells of olive endocarp.

The water-soluble extract is partly removed by the washing to which it is subjected, and thus, as pointed out by Clayton,[12] the higher the price and the finer the appearance, the less the proportion of oleo-resinous constituents. In other words, an excessive amount of

washing produces an effect similar to that found in exhausted ginger. Furthermore, it should be stated that on the keeping of ginger the contents of the secretion cells are oxidized and changed in color, as well as rendered insoluble in such solvents as alcohol, ether, acetone, glacial acetic acid, potassium hydrate solution, and chloral hydrate; whereas, in the recently dried material, in the fresh rhizome and in preserved ginger the contents are of a distinct light yellow or yellow color, the oil is in the form of globules, and the contents are easily removed by means of any of the foregoing solvents. It would thus appear that the fresher the ginger the better it is in quality.

While in the past a number of substances have been used in the adulteration of ginger, at the present time apparently exhausted ginger is chiefly used, its deficiency in pungency being made up by the addition of a small amount of capsicum or Cayenne pepper. In the examination of ground ginger for the detection of exhausted ginger or other adulterants, the following points should be borne in mind:

1. Physical appearance. In powdered ginger the material is more or less uniform and granular, whereas in the exhausted powder the fibrous character of the material is especially manifest. The color of exhausted ginger is considerably lighter; the odor is strikingly less aromatic and the taste is less pungent, unless capsicum has been added, in which case the characteristic pungency of this condiment is evident.

2. When ether-extracted ginger is dropped on the surface of water, the particles are not distributed rapidly over the surface, and show a tendency to form a scum on the water, as is the case with wheat flour.

3. On adding sulphuric acid to exhausted ginger, a greenish-brown color at first develops, which becomes darker, the reagent itself not being colored.

4. With phloroglucin the stone cells of capsicum (*Fig. 5, y*) turn to a cherry-red, as also the lignified cells of soap bark. The cells of the sarcocarp of capsicum containing red chromoplasts are readily detected when the material is mounted in chloral or fixed oil.

5. When ginger has been exhausted with water or dilute alcohol, a comparatively larger number of the starch grains have bursted or have a swollen appearance at one end, and in among the grains are

particles of starchy material formed from the altered starch grains. When viewed under the micro-polariscope, while the cross may appear to be less distinct in some of the grains, they do not for the most part seem to have lost their anisotropic character, or to have been changed in constitution.

CHEMICAL EXAMINATION.

A number of excellent papers on the chemical examination of ginger have been published abroad, one of the most important of these being the one by Reich,[10] in which the various commercial sorts as well as exhausted ginger are considered. The most complete series of analyses that have thus far been made in this country is that published by Winton and Mitchell.[11]

The commercial gingers already enumerated were also examined chemically. The methods followed were those recommended by the Association of Official Agricultural Chemists, with the exception of that recommended for the determination of starch, which was estimated according to Allihn's original method for the determination of dextrose.

The following data were obtained in the examination of samples of known purity:

TABLE No. 1.

	Total Ash.	Ash Insoluble in 10 per cent. Hydrochloric Acid.	Cold Water Extract.	Volatile Ether Extract.	Non-Volatile Ether Extract.	Alcoholic Extract.	Crude Fiber.	Starch by Direct Acid Conversion.	Lime as Calcium Oxide.
African	5.74	1.15	12.62	7.17	8.49	7.20	2.62	55.07	0.12
Calcutta	7.47	2.02	14.20	3.06	6.50	6.40	5.46	47.89	0.13
Calicut	5.64	0.55	13.08	4.62	6.42	7.76	1.64	48.77	0.33
Cochin	6.43	0.85	14.30	7.03	6.68	8.04	3.06	52.00	0.58
Jamaica	3.88	0.45	15.54	3.23	7.30	5.80	1.44	58.97	0.17
Japan	6.16	0.69	14.40	7.39	7.01	10.48	1.60	55.97	1.68

The following figures were obtained in the examination of the ash of coarsely ground gingers of known purity. All of the figures given represent the average of two samples, except in the case of Calcutta ginger, in which the figures are the average of those obtained in the examination of four samples.

TABLE No. 2.

	Total Ash.	Insoluble Ash.	Lime as Calcium Oxide.
African	5·29	1 35	0·28
Calcutta	5·83	1 07	0·18
Calicut	5·47	0·57	0·16
Cochin	5·60	0·55	0·69
Jamaica	3·56	0·29	0·09
Japan	5·22	0 38	1·02

The following table shows the averages of the figures obtained in the partial analysis of from four to six samples of gingers of known purity:

TABLE No. 3.

		Total Ash.	Insoluble Ash in 10 per cent. Hydrochloric Acid.	Starch by Direct Acid Conversion.	Alcoholic Extract.
African	Maximum	5·74	1·29	57·09	7 20
"	Minimum	5 60	1 06	48 99	5·68
"	Average	5·64	1·16	53·71	6 36
Calcutta	Maximum	7·75	2·31	60·75	6·40
"	Minimum	7·14	2·02	47·89	5·28
"	Average	7·45	2·15	52·60	5·69
Calicut	Maximum	5·64	0·69	48·77	8·16
"	Minimum	5·51	0·55	48·33	7·00
"	Average	5·56	0·61	48 55	7·64
Cochin	Maximum	6·43	0·92	52·00	8·04
"	Minimum	6·31	0·79	40·39	5·40
"	Average	6·36	0·86	44·40	6·32
Jamaica	Maximum	4·15	0·45	62 97	5·80
"	Minimum	3·72	0·16	43·64	4·32
"	Average	3·90	0·24	56·42	4·95
Japan	Maximum	6·40	0·72	55·97	10·48
"	Minimum	6·02	0·61	39·99	6·96
"	Average	6·14	0·66	50·60	8·37

The following data were obtained in the examination of authentic samples of African and Calcutta gingers:

TABLE No. 4.

	Total Ash.	Insoluble Ash in 10 per cent. Hydrochloric Acid.	Crude Fiber.	Starch by Direct Acid Conversion.
1. African	6.09	0.86	6.88	52.50
2. "	5.09	0.34	—	62.66
3. "	5.16	0.35	—	—
4. "	6.00	0.86	7.44	53.14
5. "	5.93	0.80	—	—
6. Calcutta	6.94	1.68	4.84	54.97
7. "	7.61	2.17	4.80	55.80

The following data were obtained in the examination of twenty-three samples of pure ground ginger:

TABLE No. 5.

	Total Ash.	Insoluble Ash in 10 per cent. Hydrochloric Acid.	Crude Fiber.
Maximum	8.40	2.19	6.80
Minimum	6.08	1.04	6.10
Average	6.78	1.45	6.37

The following figures were obtained in the examination of commercial gingers bought on the market:

TABLE No. 6.

	Total Ash.	Water Soluble Ash.	Insoluble Ash in 10 per cent. Hydrochloric Acid.	Crude Fiber.	Cold Water Extract.	Alcoholic Extract.	Volatile Ether Extract.	Non-Volatile Ether Extract.	Lime as Calcium Oxide.	Starch by Direct Acid Conversion.
1	6.93	2.52	1.62	6.04	11.28	6.84	1.91	7.09	0.41	46.12
2	7.05	2.84	1.54	8.14	12.64	6.16	2.63	7.23	0.50	45.27
3	6.26	2.98	1.23	5.54	12.02	7.84	1.90	8.19	0.30	45.76
4	6.52	2.87	1.18	4.14	11.94	7.60	1.45	6.85	0.44	52.76
5	5.00	2.66	0.50	5.17	11.92	7.52	1.90	8.22	0.44	45.84
6	5.02	2.70	0.41	5.70	13.20	5.24	1.38	8.75	—	45.80
7	2.78	0.95	0.39	5.72	6.62	4.68	1.63	3.87	0.52	46.40

An examination of the figures given in Table 6 shows that all of the samples of commercial powdered ginger conform to the Government standard for starch and lime. All, except No. 2, contain less than 8 per cent. of crude fiber. They all come within the limits for insoluble ash, although the total ash is too high in Nos. 1, 2, 3 and 4. The samples are all lower in volatile ether extract than any of the authentic samples, analyses of which are given in Table 1, and Nos. 1, 4 and 5 show less cold-water extract. No. 7 was obtained as exhausted ginger, and is notably low in water-soluble ash, cold-water extract, alcohol extract, volatile ether extract and non-volatile ether extract.

MICROSCOPICAL EXAMINATION OF SAMPLES OF COMMERCIAL POWDERED GINGER.

The foregoing samples of commercial powdered gingers were also examined microscopically. Nos. 1 and 2 show the presence of Cayenne pepper and of olive endocarp (*Fig. 5*).

No. 4 contained aggregations of starchy material about 0·5 mm. in diameter, in which were distributed reddish oil globules resembling those of capsicum, which, together with the pungency characteristic of capsicum, suggested the addition of tincture of capsicum.

No. 5 contained numerous fragments, about 0·5 mm. in diameter, with polygonal non-lignified cells containing numerous yellowish-brown globular masses from 20 to 30 μ in diameter.

Nos. 3, 4, 5 and 6 all contained a considerable amount of fibrous material, as well as thick-walled isodiametric cells which were strongly lignified. While the presence of this foreign material may have been due to failure in properly garbling the ginger rhizomes, the amount was such as to warrant one in looking upon the samples with suspicion.

No. 7, which was obtained as an exhausted ginger, contained numerous fragments of quillaja or soap bark, as also the typical calcium oxalate crystals of quillaja.

SOME GENERAL CONCLUSIONS.

In considering the data obtained in both the microscopical and chemical examination of the samples of commercial powdered ginger and those of known purity, the conclusion is reached that commer-

cial powdered ginger, as, for example, samples 5, 6 and 7 in Table 6, may conform to the official standards, and yet be adulterated or contain exhausted ginger, or on the other hand be pure and yet vary slightly in the percentage of ash, as given in Tables 1, 4 and 5.

The comparatively high percentage of ash in Calcutta ginger may probably be accounted for by the larger amount of cork and the number of sclerenchymatous fibers in the fibrovascular bundles. That this is true is also shown by the fact that the percentage of crude fiber in Calcutta ginger is higher than in the other gingers examined (Table 1). While the analyses of Calcutta and African ginger, as given in Table 4, do not strictly bear out this assumption, it is seen that in the case of African ginger there is a ratio between the crude fiber and total ash, *i. e.*, the higher the percentage of crude fiber the higher the percentage of ash. The same holds with Cochin ginger, where the fibrovascular bundles are large and numerous, notwithstanding the amount of cork is small. In the case of Japan ginger, the rather high ash is accounted for by the fact that it is a limed ginger.

From the observations herein recorded, it would seem that there should be different standards for ash in the different sorts. In other words, it would probably be better to require the ash in Jamaica ginger to be between 4 and 5 per cent. and that for Calcutta ginger to be between 7 and 8 per cent., than to have a uniform standard of 6 per cent.

In forming an opinion as to the quality of powdered or ground commercial ginger, the following points should be borne in mind:

1. The powder should be uniformly granular and have a pronounced characteristic aromatic odor and a characteristic pungent taste.

2. On treatment with sulphuric acid, the particles of genuine ginger become of a reddish-brown color, which changes rapidly to dark brown and finally to purplish-brown.

3. With phloroglucin and hydrochloric acid, few or none of the fragments should be stained a cherry-red color.

4. Of the official standards, those for the total ash and crude fiber are the most important. The latter is of special importance if the microscopic examination with phloroglucin shows the presence of any lignified tissues.

5. The volatile ether extract should not be less than 3 per cent.

LITERATURE CITED.

[1] George Watt: A Dictionary of Economic Products of India, 6, Part 4, p. 358.

[2] Bentley and Trimen: Medicinal Plants, 4, Monograph 270.

[3] Berg und Schmidt: Officinel Gewächse, Taf. XXXIV, b.

[4] Engler und Prantl: Die natürlichen Pflanzenfamilien, II. Teil, 6. Abteilung p. 26.

[5] F. B. Kilmer: AMERICAN JOURNAL OF PHARMACY, 70 (1898), p. 75.

[6] P. L. Simmonds: Tropical Agriculture, p. 497.

[7] Arthur Meyer: Wissenschaftliche Drogenkunde, Part II, p. 64.

[8] A. Tschirch und O. Oesterle: Anatomischer Atlas, Lief. VI, p. 109, Tafel XXVI.

[9] Joh. Buchwald: *Zeitschr. f. Untersuchung d. Nahr.- u. Genussmittel*, 2 (1899), p. 947.

[10] R. Reich: *Zeitschr. f. Untersuchung d. Nahr.- u. Genussmittel*, 14 (1907), p. 549.

[11] A. L. Winton and W. L. Mitchell: Connecticut Agricultural Experiment Station, Twenty-second Annual Report (1898), p. 144.

[12] E. G. Clayton: *The Analyst*, 24 (1899), p. 122.

NOTES ON "PHYSIOLOGICAL TESTING."[1]

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I was asked to speak on the question of physiological testing, I suppose, because of my former connection with certain of the large drug firms. This connection has given me a rather closer interest in the subject than is usual with pharmacologists in this country, and I had planned to write a series of papers on these methods. The first of this series—the one on the testing of suprarenal glands—has already been published,[2] but it is now a question as to whether I shall be able to complete the series.

The use of animals for testing drugs and chemicals is a method of very old origin and long antedates the use of the term "physio

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[1] Read before the Baltimore Branch of the American Pharmaceutical Association, May 21, 1908.

[2] Crawford, A. C. Use of the Suprarenal Glands in the Physiological Testing of Drug Plants. United States Department of Agriculture, Bureau of Plant Industry, Bulletin 112.

logical testing." This term is, I think, so widely known because of its exploitation by certain of the large drug firms. It has come, in the minds of certain people, to mean a fairly quantitative test of drug preparations on animals. Kobert prefers the use of the term "biological testing," as it has a wider significance, and since the term may be used in reference to the testing qualitatively of chemicals on any form of life, while the term "biological assay" seems more desirable for the quantitative determination by this method.

It has been well recognized that many of the drugs and chemicals cannot be standardized by the ordinary chemical methods, and for this reason they have been tested on animals. There are certain classes of drugs, which, at the present time, can be only thus standardized; for example, the members of the digitalis group, cannabis indica, ergot, antitoxines and the preparations of the ductless glands. As yet we have no other method of testing yohimbin, curare, abrin, ricin, jequirity,[1] saponins, etc. Kobert practically admits that the chemical test is unsuited for the recognition of aconitine, and that such tests fail for small quantities of picrotoxin, etc. Dixon[2] claims that "lobelia can be standardized very accurately by its effect upon blood pressure and its subsequent paralytic action on certain nerve cells." Then again, there are preparations which, while they can be standardized by chemical means, may with advantage be controlled by the physiological test, at least qualitatively; thus, cocaine produces characteristic anæsthesia of the mucous membranes, and atropine produces dilatation of the pupil, and the addition of these tests may render the chemical ones more certain. Others again may be tested by either chemical or biological methods, according to circumstances. Kobert, under certain conditions, prefers the test for arsenic by means of *Penicillium brevicaule* to the Marsh test, although it must be admitted that certain arsenic compounds by this test fail to respond.

ADRENAL GLANDS.

We, Baltimoreans, should be especially familiar with these glands because the first chemical work in this country was done in this

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[1] Scholtz, K. Werthbestimmung d. Jequiritols u. des Jequiritol-Heilserum durch Thierexperimente. *Arch. f. Augenheilkunde*, Vol. 55, p. 209. 1906.

[2] Dixon, W. E. Bio-Chemical Standardization of Drugs. *Pharm. Journ.*, Vol. 75, p. 157. 1905.

city in Professor Abel's laboratory. The best-known preparation of the active principle of these glands which is on the market is that bearing the name of Takamine. Abel has shown, however, that this preparation is not chemically pure. Aldrich, Abel's former associate, has obtained an extremely pure form of this body, and retained Takamine's name; but its production by Aldrich's method is not commercially possible. This adrenalin of Aldrich and Abel's later product, Epinephrin, are probably identical.

There have been numerous attempts to assay these preparations by color reactions produced by iodine and iron chloride; but, while these are fairly serviceable with the pure principle, when used with preparations of the glands themselves, which are colored, they are very misleading. It is admitted by most investigators that the physiological test is the most convenient method of assaying them. Objections have, however, been raised on account of the extreme delicacy of the test.

The method which has been advocated is that by means of the frog's eye or that of Meyer by noting the contraction of strips of muscle while placed in the solution to be tested. In this country we usually assay such preparations by determining the minimum quantity of the solution which will cause a rise in the systemic blood pressure of a narcotized dog with the vagi nerves cut, and comparing this rise with that produced by a definite amount of the pure active principle. The difficulty with all methods is to decide what preparation to use as a standard. The ordinary commercial adrenalin contains a certain amount of extraneous matter (phosphates), so that to standardize preparations accurately a high grade of adrenalin, such as that of Aldrich, or Abel's Epinephrin, should be used.

A method which offers a future is the standardization against a nitrite solution, such as recommended by Cameron. He has shown that a definite amount of nitro-glycerine will neutralize the action on the blood pressure of a definite amount of adrenalin. The physiological test on blood pressure runs within about 5 per cent. error. These methods have been discussed in full in my paper on the suprarenal glands.

The question as to the standardization of the thyroids and pituitaries has not yet been raised, but will no doubt soon be opened. These glands offer peculiar difficulties for the biological assay. As

to the thyroids, the only test yet offered is that of Hunt.[1] The pituitaries cause a rise in blood pressure, and this test may perhaps be used. Unfortunately, after a few injections of pituitary extracts, the circulatory organs acquire a certain immunity to them and fail to respond by a rise in blood pressure.

ERGOT.

There has been an endless amount of discussion as to the active principle of ergot and its assay. The chemical work up to the present time has been one of utmost confusion. Recently, Barger, Carr and Dale,[2] of the Wellcome Research Laboratory, have isolated an amorphous base, ergotoxine, which forms crystalline salts, and a crystalline base, ergotinine, corresponding to Tanret's crystalline ergotinine. This forms amorphous salts. Ergotoxine has been shown to possess the action of ergot on the uterus, the cock's comb, and to cause a rise in blood pressure. Ergotinine is said to be inactive. The total alkaloidal content is about 0·1 per cent.

Simultaneously with the appearance of this work, Kraft[3] independently published almost identical results, but named his alkaloidal bodies differently from the Wellcome Research workers. These investigators, however, finally agreed that they were working with the same compounds. The presence of more than one basic body had been noted several years ago by Tanret and still earlier by Wenzell. The preparations of Kobert and Jacobi are not chemically pure bodies, but are mixtures in varying degrees of the active principle with more or less inert matter. Clavin, the principle isolated by Vahlen,[1] is reported inactive by Cushny,[2] Dale and Kehrer.

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[1] Hunt, R. Probable Demonstration of Thyroid Secretion in the Blood in Exophthalmic Goiter. *Jour. Amer. Med. Assoc.*, Vol. 49, p. 240. 1907.

[2] Barger, G. Ueber Mutterkornalkaloide. *Arch. d. Pharm.*, Vol. 245, p. 235. 1907.

Barger, G., and Dale, H. H. Ergotoxine and Some Other Constituents of Ergot. *Bio-Chem. Jour.*, Vol. 2, p. 240. 1907.

Barger, G., and Carr, F. H. Alkaloids of Ergot. *Jour. of Chem. Soc.*, Vol. 91, p. 337. 1907.

Barger, G., Carr, F. H., and Dale, H. H. An Active Alkaloid from Ergot. *Brit. Med. Jour.*, 1906, Vol. 2, p. 1792.

Dale, H. H. On Some Physiological Actions of Ergot. *Jour. Physiol.*, Vol. 34, p. 163. 1906.

[3] Kraft, F. Ueber das Mutterkorn. *Arch. d. Pharm.*, Vol. 244, p. 336. 1906.

Dale has shown that ergotoxine will cause a marked rise in blood pressure in decerebrized cats. Dixon[3] claims the action of ergot on the blood pressure to run parallel to its action on the uterus. I have found that the alkaline ether shaken from ergot gives a persistent rise in blood pressure in narcotized dogs with cut vagi, and believe the trouble experienced by other experimenters (Sollman and Brown)[4] is probably due to the fact that the inorganic salts and perhaps cholin were not removed in their experiments. It seems at first sight to offer a possible method of standardizing these preparations to use Dale's method and note the amount of ergot solution necessary to cause a reversal in action of a definite amount of adrenalin. Dale, however, believes that there is more than one principle involved in this action. If this is true, then we cannot as yet standardize entirely with reference to ergotoxine.

Up to the present it has seemed to me that all we can do is to rely on the bluing of the cock's comb by either the injection or the feeding of ergot preparations. My own method has been to inject subcutaneously 5 c.c. of the fluidextract into a rooster, and after about an hour's interval the comb and wattles will become markedly blue and cold, provided the preparation is active. This bluing passes off during the course of twenty-four hours. Some of the large firms use the method of feeding ergot preparations to Leghorn roosters which have been starved for twenty-four hours. These animals are then fed 15 to 30 c.c. of the fluidextract, after evaporating off the alcohol. Bluing of the combs and wattles occurs in a few hours. The objection I see to this test is the fact that ergot preparations are often irritating and may not be absorbed, and thus

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[1] Vahlen, C. Clavin, ein neuer Mutterkornbestandtheil. *Arch. f. exper. Path.*, Vol. 55, p. 131. 1906.

[2] Cushny, A. R. On the Movements of the Uterus. *Jour. Physiol.*, Vol. 35, p. 19 1906.

[3] Dixon, W. E. Biochem. Standardization. *Pharm. Jour.*, Vol. 75, p. 157. 1905.

[4] Sollman, T., and Brown, E. D. Intravenous Injection of Ergot. *Jour. Amer. Med. Assoc*, Vol. 45, p. 229. 1905.

A good handling of the question of the action of ergot on the circulation can be found in E. Jolly. Die Einwirkung des Mutterkorns auf die Circulation. Göttingen. 1905.

produce no action. I noted that, after repeated injections of ergot into cocks, these animals showed marked hypertrophy of the comb, and gangrene occurred at the site of injection, an observation agreeing with those of Ferè[1] and Santesson.

The chemical test of the activity of ergot I think unreliable. Dr. Dohme[2] and I made some years ago a statement that the Keller method of assay for cornutine was a fairly accurate method of standardizing ergot. I shall have to modify my part of this statement by saying that unquestionably, so far as I have seen, all the active principle which causes bluing of the cock's comb is shaken out by alkaline ether, in the Keller method, and, in fact, this extract seems to be more active than the original fluidextract of ergot itself; but the mere weighing of this evaporated residue could not give any absolute idea as to the quantitative activity of ergot, because of the extraneous matter present. It seems that besides the active alkaloid also the inactive one is present in the ether extract, and interferes thus with the results.[3]

Barger and Dale[4] believe the cornutine of Keller to be a mixture of ergotinine with 25 per cent. ergotoxine. One of the strong arguments urged by Santesson against the possibility of Keller's cornutine being the active principle of ergot was the fact that in old, presumably inactive ergots, the assay for cornutine often ran relatively high. This now can be explained, as we know the active alkaloid can be readily converted into the inactive one and *vice versa.*

I think the ideal method of testing preparations would be to standardize drugs for the use to which they are to be put in medicine. As ergot is used almost entirely to promote uterine contractions, under these conditions the satisfactory tests would be the standardization by its action on the uterus of some of the lower animals.

This method was used by Diez in 1831. I have collected numer-

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[1] Ferè, C. Note sur une hypertrophie provoquèe de l'ergot de coq. *Comp. rend. hebd. Soc. de Biol.*, 1900, Vol. 52, p. 474.

[2] Dohme, A. R. L., and Crawford, A. C. Active Principle of Ergot. *Proc. Amer. Pharm. Assoc.*, Vol. 74, p. 503. 1902.

[3] Santesson, C. G. Ueber die Wirkung des Cornutin Keller und einiger anderer Secale-extracte. *Skand. Arch. f. Physiol.*, Vol. 13, p. 107. 1902.

[4] Barger, G., and Dale, H. H. Ergotoxine and Some Other Constituents of Ergot. *Bio-Chem. Journ.*, Vol. 2, p. 277. 1907.

ous data on this method, but have recently found that Kehrer[1] has developed it, using the isolated uterus from cats, and claims it to be the best method yet proposed. He uses as his standard 0.01 gramme of ergot in 200 c.c. of Ringer solution as his minimal active dose. According to this test, ergots preserved one year in drug stores become seven or eight times weaker, while after two years, preservation they become fifteen times weaker than originally. Kobert and Gruenfeld[2] showed, by testing on the cock's comb, that ergot lost its activity completely in six months under ordinary conditions. Kehrer, by his test, noted that aqueous extracts of ergot began to lose their activity in a few hours. According to Kobert, no fluid preparation of ergot preserves its activity over twelve months. Perhaps a part of such loss in activity is due to the action of microorganisms.[3] It is, however, known that Bischofberger,[4] as a result of certain clinical experiments on women, claimed that ergot two years old was still active; but the clinical testing of drugs is often apt to be fallacious, as one is unable to control all the conditions, and clinicians are well acquainted with the fact that uterine contractions often appear independent of any drug used.[5]

CANNABIS INDICA.

The chemistry of cannabis is another dark spot, and all that we can say is that at present the active principle seems to be a resinous body, cannabinol, which was obtained by Fraenkel[6] by distillation

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[1] Kehrer, E. Der überlebende Uterus als Testobject für die Wertigkeit der Mutterkornpräparate. *Arch. f. exper. Path.*, Vol. 58, p. 366. 1908. Compare also the negative results of E. M. Kurdinowski, Physiol. u. pharmakol. Versuche an d. isolirter Gebärmutter. *Arch. f. Physiol.*, Physiol. Abtheil. Suppl. Band., p. 372. 1904.

[2] Gruenfeld, A. Beitr. z. Kenntniss d. Mutterkornwirkung. Arbeit. d. pharmakol. Institut. z. Dorpat, Vol. 8, p. 149, etc. 1892. Kobert, R. Present State of the Ergot Question. *Practitioner*, Vol. 35, p. 416. 1885.

[3] Leopard, H. Ueber d. Vorkommen von Mikroorganismen in Ergotinlösung. Dissert. Würzburg, 1887.

[4] Bischofberger, A. Geburts-klin. Untersuch. über. Haltbarkeit d. Mutterkorns. Dissert., p. 45. Bern, 1897.

[5] For literary details on the ergot question consult Krysinski, S. Pathol. u. krit. Beitr. z. Mutterkornfrage. 1888.

[6] Fraenkel, S. Chemie u. Pharmakol. d. Haschisch. *Arch. f. exper. Path.*, Vol. 49, p. 266. 1903.

in extremely high vacuum. Fraenkel found that this pure body would not act on subcutaneous use. We have no chemical method of standardizing cannabis, and the isolation of the body is attended with considerable difficulty, so that the method we use is to feed these preparations to dogs, and note the minimum quantities which will produce incoördination in their movement. Dogs thus fed will become unsteady in their legs and wobble from side to side. All dogs, even of the same weight, do not respond the same to cannabis, so that it may be necessary to feed the drug to a number of dogs and select the one which responds best and use it as the standard for the systematic testing of such preparations. This test has been reported on in full by Dr. Houghton in the January number of the *Therapeutic Gazette*. Ten to fifteen milligrammes per kilo of the extract should produce incoördination in one hour. Chevalier[1] has also recently experimented on this subject, and the report of Famulener and Lyons,[2] which is well worth perusal, furnishes details accessible to us. These latter authors claim that the fluidextract of cannabis underwent little deterioration in a twelve-months' preservation.

Dixon uses in his tests cats weighing about 2½ kilos. He injects subcutaneously these animals with 10 minims of the tincture diluted with the same amount of water. In a short time their gait becomes unsteady, the reflexes are increased in activity and the pupils dilate, if the preparation is active.

Houghton calls attention to the low toxicity of cannabis, and the question arises whether any very exact quantitative assay is necessary. Wood[3] and Houghton have made the important observation that American-grown cannabis has the activity of cannabis grown in India.

DIGITALIS.

The group of digitalis, strophanthus, squill, etc., is the most important one we physicians have to use, and urgently demands

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[1] *Bull. gén. de Therap.*, Vol. 155, p. 18. 1908. (Seen only in reference.)

[2] Famulener, L. W., and Lyons, A. B. Physiological Assay of Cannabis Indica. *Proc. Amer. Pharm. Assoc.*, Vol. 51, p. 240. 1903.

[3] Wood, H. C. On the Medicinal Activity of the Hemp Plant as Grown in North America. *Proc. Amer. Philos. Soc.*, Vol. 11, p. 226, 1871.

An interesting article by Czerkis on Cannabinol can be found in the *Pharmaceutische Post*, 1907, pp. 49, 69, 97.

standardizing. Naunyn[1] made the assertion that he would not care to be a physician without digitalis. Focke,[2] Edmunds, Kobert, Fraenkel, Bennefeld and others have recently called attention to the marked variation in strength of digitalis leaves. In fact, Ott says that the leaves of digitalis grown in Bohemia are too toxic for clinical use. Unfortunately the appearance of the leaves does not give any indication as to their activity.

Dixon[3] says: "For my part I unhesitatingly express the belief that many hundreds of patients die annually from digitalis and allies not possessing the virtues which are required of them." The clinical testing of such preparations on man may not always yield satisfactory ideas as to their real activity, as Loewy[4] has shown that many of these preparations are injured by the normal acidity of the stomach. Focke[5] showed by physiological tests that the leaves lost much of their activity by ordinary keeping. He believes that light has little to do with this deterioration, and that it is a question of carefully drying the leaves and then keeping them in air-tight vessels protected from moisture. Thus Wang, who tested leaves kept in such a manner for two years, found they had the same toxic value for frogs as fresh leaves, while Focke kept such leaves unchanged for three years. Wolff[6] found that it was desirable to dry the leaves in vacuo at a definite temperature, as the ordinary drying in air might be injurious to their activity.

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[1] *Muench. med. Woch.*, 1904, p. 1413.

[2] Focke, C. Ueber d. jahreszeitl. Schwankungen in d. Stärke d. officinell. Folia Digitalis, *Ther. d. Gegenw.* n. s., Vol. 4, p. 44. 1902. Ott. Verhandl. d. Kongresses f. Innere Med., 1901, p. 89. Fraenkel, A. Ueber d. physiol. Dosirung von Digitalispräparaten. *Ther. d. Gegenw.* n. s., Vol. 4, p. 112, 1902. Fraenkel, A. Exper. Untersuch ü. d. Wirksamkeit d. verschied. Digitalispräparaten. *Charité Annalen*, Vol. 6, p. 207. 1881. Edmunds, C. W. Standardization of Cardiac Remedies. *Jour. Amer. Med. Assoc.*, Vol. 48, p. 1744. 1907. Bennefeld, F. Ueber Digitalistincturen. Dissert. Göttingen, 1881. Lutzkaja, S. Ueber d. Wirkungswert d. Folia Digitalis. *Arch. Internat. de Pharmakodynamie*, Vol. 18, p. 77. 1908.

[3] Dixon, W. E. Drug Fallacies. *Brit. Med. Jour.*, Vol. 2, Nov. 1906.

[4] Loewy, J. Ueber d. Bedeutung d. Reaktion d. Digitalisinfuses f. seine Wirksamkeit. *Wien. klin. Woch.*, Vol. 19, p. 1157. 1906.

[5] Focke, C. Physiol. Wertbestimmung d. Digitalisblätter. *Arch. d. Pharm.*, Vol. 241, p. 140. 1903.

[6] Wolff, A. Ueber d. Physiol. Dosirung von Digitalispräparaten. *Ther. d. Gegenw.* n. s., Vol. 4, p. 423. 1902.

Our Pharmacopœia demands that only leaves of the second year's growth be used, and this demand is supported by the experiments of Focke, who found the first year's leaves weaker toward frogs than those of the second year's growth. However, Merck's Report (1907, p. 253) quotes Haynes to the effect that the leaves of the first year are as active as those of the second year, provided they are grown under the same conditions.

Fraenkel has noted that the infusion of digitalis varied in strength from 100 to 275 per cent., while tinctures varied from 200 to 400 per cent. Tinctures of digitalis, when exposed to the light, lost about one-half of their original strength in one year.[1] The infusion loses one-half of its activity in twenty-four hours (Loewy). The addition of a small amount of sodium carbonate is claimed to preserve the infusion for several days.[2]

Our chemical knowledge of these drugs is extremely deficient. There have been a number of bodies isolated from digitalis: digitalin, digitalein, digitophyllin, digitoxin, etc., and as decomposition products of these, digitoxiresin and toxiresin. Haynes[3] and Dixon have reported that many of these principles are inactive, and Haynes says: "These so-called active principles require standardization even more than the galenical preparations." While at one time we thought digitalin was the active principle, now it is thought that digitoxin is the real principle, and attempts are made to standardize the preparation by determination of the digitoxin present.[4]

For this assay the method of Keller, or Keller's method modified by Fromme, is usually used. Barger and Shaw[5] and Ziegenbein[6] have shown by experiments on frogs that the toxicity of the digi-

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[1] Focke, C. Ueber d. prakt. Wert unserer Digitalistincturen. *Deutsch. Aerzt. Ztg.*, Vol. 6, p. 292. 1904.

[2] Focke, C. Wie kann man ein Digitalisinfus bis zu seinem Verbrauch haltbar machen? *Med. Klinik*, Vol. 3, p. 484. 1907.

[3] Haynes, G. S. Pharmacological Action of Digitalis, Strophanthus and Squill on the Heart. *Bio-Chem. Jour.*, Vol. 1, p. 63. 1906.

[4] Reed, E. D., and Vanderkleed, C. E. Standardization of Preparations of Digitalis by Physiological and Chemical Means. *Amer. Jour. Pharm.*, Vol. 80, p. 110. 1908.

[5] Barger, G., and Shaw, W. V. Chemical and Physiological Assay of Digitalis Tinctures. *Yearbook of Pharmacy*, 1904, p. 541.

[6] Ziegenbein, H. Werthbestimmung d. Digitalisblätter. *Arch. d. Pharm.*, 1902, Vol. 240, p. 454.

talis preparations does not correspond to the toxicity of the digitoxin present, and experiments on dogs show a similar disagreement.[1] Vanderkleed, however, claims some degree of parallelism between the digitoxin content and the toxicity of digitalis on guinea pigs. The weight of evidence, however, is that digitalis leaves do not owe their activity to any one yet discovered principle.

These preparations are usually standardized by merely determining their toxicity on frogs. Houghton has reported in the National Standard Dispensatory the method of performing this test. He used the normal lethal dose of 0.0015 gramme per gramme frog for the fluidextract digitalis and 0.00015 gramme for the fluidextract strophanthus, 0.011 gramme for fluidextract squills. Haynes used as his standard that 2½ minims of a tincture of digitalis should kill a frog of 20 grammes weight in three hours, while ¼ minim of tincture of strophanthus should kill a frog weighing 17 grammes. Others, again, recognizing that the characteristic action of this group is the systolic stoppage of the frog heart, have demanded that the preparation be standardized with reference to the quantity which shall cause systolic stoppage of the ventricle within a certain period, some say twenty minutes, some an hour or more.[2] Famulener and Lyons, in the Proceedings of the American Pharmaceutical Association for 1902, have described this method in full. The exact period at which systolic stoppage occurs is at times hard to decide.[3] In none of the work, as far as I have been able to find, is there any accurate description of the frogs used. In fact, the old classification of frogs is very unreliable, and frogs vary so much in their response to drugs

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[1] Wood, H. C., Jr. Does Digitoxin Represent the Therapeutic Virtues of Digitalis? *Amer. Jour. Pharm.*, 1908, p. 107.

[2] Ziegenbein, H. Werthbestimmung der Digitalisblätter. *Arch. d. Pharm.*, 1902, vol. 1, p. 454.

Bührer, C. Ueber d. Grenzen d. Wirksamkeit einiger toxisch. Fluidextracte. *Corresp. d. Schweizer Aerzte*, 1900, Vol. 30, p. 617. Siebert. Werthbestimmung von Digitalis und Strophanthus durch Prüfung an Froschherz. *Berl. klin. Woch.*, Vol. 40, p. 813. 1903. Dixon, W. E. Bio-Chemical Standardization of Drugs. *Pharm. Jour.*, Vol. 75, p. 156. 1905. Focke, C. Die physiol. Werthbestimmung d. Digitalisblätter. *Arch. d. Pharm.*, Vol. 241, p. 128. 1903; Ueber den gleichmässig. Wirkungswert von gut präparirtem und gut aufbewahrtem Digitalisblätterpulver. *Ther. d. Gegenw.*, 1904, p. 250; Zur physiol. Wertheinstellung d. Digitalisblätter. *Ther. d. Gegenw.*, 1904, p. 527.

[3] Wang, E. Werthbestimmung d. Digitalisblätter. Festschrift Olof Hammarsten gewidmet. *Upsala*, 1906, p. 7.

according to species, sex, seasons, whether summer or winter, and also with the temperature at which they are kept, that I think frogs unsatisfactory. Then again, large amounts of inorganic salts present in the extracts would act injuriously on frogs. Many of the observers forget the original investigations of Schmiedeberg, who found that only so-called Rana temporaria showed the characteristic systolic stoppage of the heart from digitalis in a typical manner. Masi noted that digitalin arrested the frog heart in systole, while digitonine caused diastolic arrest of the heart; and further, that if the frogs were immersed in 0·75 per cent. saline solution at 32°[1], digitaline would then cause diastolic stoppage, and Ziegenbein has found that while small doses of digitoxin cause systolic arrest of the heart, often large doses do not.

In one experiment performed in summer, Focke noted that the ventricle at times stopped in diastole and, therefore, urged that the temperature of the room, in which such experiments are carried out, should be within certain limits.[2]

Dr. Reed, of Philadelphia, has made an important advance by using guinea pigs, animals which are more resistant to injury. He apparently uses a dose of 0·6 to 1 c.c. of the tincture per 240 grammes of guinea pig as his standard.

While these methods are all very desirable, the mere determining of the toxicity of the preparation does not to my mind determine its medicinal value. For example, it has been well recognized that the reported active principles readily decompose into digitoxiresin, toxiresin, etc., which are very toxic bodies. If we had a slightly larger amount than normal of decomposition products, we would have an extremely high toxicity, but this would not necessarily mean a high medicinal action.

Sowton[3] has improved the method of testing such preparations by using the mammalian heart. He perfuses rabbit hearts isolated by the Langendorff method with tincture of digitalis 1 to 200,

[1] Masi, G. B. Sull Azione fisiol. della Digitalina. *Riforma Med.*, Vol. 6, pt. 1, p. 741. 1890. Data on our American frogs can be found in Mary Dickerson's Frog Book, while details as to the European species may be seen in G. A. Boulenger's "The Tailless Batrachians of Europe." *Ray Soc.*, 1897.

[2] Focke, C. Weiteres z. physiol. Prüfung d. Digitalisblätter. *Arch. d. Pharm.* Vol. 245, p. 646, 1907.

[3] Sowton, S. C. M. Some Experiences in the Testing of Tincture of Digitalis. *Brit. Med. Journ.*, 1908, Vol. I, p. 310.

Ringer's solution. This method was also tried by Haynes. The strength of these solutions is judged by the length of time necessary to cause stoppage of the right ventricle. Perhaps some of the difficulties with such experiments are due to the fact that the various principles affect different portions of the heart. Focke's method of removing the sternum in unpithed frogs should be discarded on humanitarian grounds.

Theoretically to me the proper way would be to determine the toxicity of these preparations on guinea pigs, and also the action on the isolated mammalian heart, or on the heart in situ, noting the slowing of the heart-beat[1] and the time necessary to cause stoppage, and any rise of blood-pressure, or by making use of the physiological antagonism between digitalis and the nitrites[2] in addition to the toxicity experiments. Naturally in such experiments the depressing potassium salts should be removed from the extract. The standard should be leaves carefully dried in vacuo by Wolff's method and then protected from moisture by preserving in air-tight vessels.

It is needless to add that a thorough botanical identification of the species should be made by an expert. Other species of digitalis besides the official digitalis purpurea are probably also active.

It must be confessed that the methods thus far proposed are not accurate. A long series of experiments should be made with one tincture, and checks made by diluting this to various strengths and comparing the results obtained from these known dilutions on animals.

Dixon[3] has reported that if 5 c.c. of a tincture of digitalis be placed in the stomach of an anæsthetized dog and the stomach be examined two hours later, the stomach will show signs of acute inflammation, and Haynes noted that after similar placing of tincture of digitalis no effect on blood pressure was observed. This failure in action was probably due to non-absorption. Further, Deucher[4]

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[1] Fraenkel, A. Ueber Digitaliswirkung am gesund. Menschen. *Muench. med. Woch.*, Vol. 52, p. 1537. 1905.

[2] Marshall, C. R. On the Antagonistic Action of Digitalis and the Members of the Nitrite Group. *Journ. Physiol.*, Vol. 22, 1897–8.

[3] Dixon, W. E. Manual of Pharmacology, 1906, p. 169.

[4] Deucher, P. Ueber d. Wirkung des Digitalin verum bei Circulations-störungen. *Deutsch. Archiv. f. klin. Med.*, 1896, Vol. 57, p. 34.

NOTE.—In considering Strophanthus, Hatcher's article in the *Journal of the American Medical Association* for 1907, and Santesson's article in the *Skandinavisches Archiv fuer Physiologie* for 1905 may be serviceable.

showed that by gastric digestion digitalin underwent a marked weakening, so that it can be easily seen that the responsibility for a failure of digitalis to act clinically cannot always be laid at the pharmacist's door and this is well worth remembering in these days of lawsuits.

Certain of the purgative drugs likewise cannot be satisfactorily standardized by chemical means, and the physiological test is also rather unsatisfactory, but it is better than the chemical. The emetic drugs can be assayed chemically, but can also be tested physiologically on dogs.

These tests give no indication of the activity of the drug on man, as various animals respond differently, but only as to its comparative strength.

Such, in brief, are the methods in use in the testing of galenical preparations, and as quantitative procedures much is to be desired. It must be remembered that because one firm calls a drug physiologically tested, it does not follow that the drug compares at all with another so-called physiologically tested preparation. In fact, the standards and ideas of testing of one firm may be very different from that of another, and no label "physiolocically tested" means much unless one knows the standard used. One English firm is putting out digitalis leaves and specifies them to be standardized on a basis of 1·4 grammes of the leaf as the minimal toxic dose for 100-gramme frog. Our American firms simply state "physiologically tested."

While many of these preparations may contain full alkaloidal strength, which can be determined by chemical analysis, yet it is perfectly possible that some may be too irritating for certain usage and set up purgation or emesis. As is well known, one of the problems has been to obtain a digitalis preparation which is non-irritating. This irritating action can be determined by the biological test, such as described by Houghton.[1] Again, the simple determination of the amount of alkaloids present in such preparations does not necessarily correspond to the activity of the preparation; because, as physical chemistry has shown, the presence of a large amount of colloids often interferes with the full action of certain chemical compounds. Again, the presence of certain elements increases the

[1] Houghton, E. M. Attempt to Obtain a Uniformly Active, Sterile and Non-irritating Preparation of Digitalis. *Medicine*, Vol. 9, p. 982. 1903.

activity of certain others; thus, small quantities of barium render toxic an otherwise non-toxic dose of KCNS, so that the final test must be that on animals.

The question comes up as to who shall perform such tests. Pharmacists and the practicing physician certainly would not be in a position to carry them out on account of the special training which these tests require, and it seems to me that both of these classes of gentlemen already have their hands full. The difficulty of such testing becomes apparent when we see what different results experimenters are arriving at as to the question of the toxicity of the food preservatives, and even in the case of such a well-known body as ethyl alcohol. Many of the large firms are now employing professional pharmacologists to do such work. In Germany[1] there is now a considerable movement to organize a Government Bureau for the testing of these preparations, and it will not be long before the Federal Government will be compelled to establish such a Bureau.[2] It is urgently desired that representatives of the various pharmaceutical and medical societies meet and decide upon suitable standards.

ELIXIRS OF THE NATIONAL FORMULARY.

By E. Fullerton Cook, P.D.[3]

The statements which are made in this paper of a critical character, or otherwise, are based upon actual experiments with commercial products. Where difficulties have been met with, it may be that in some instances, at least, minute quantities of foreign substances in the ingredients have caused precipitation in the liquid preparation. Further experiments will subsequently be conducted to verify the results here reported and to suggest satisfactory modifications in the several formulas.

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[1] Fraenkel, A. Ueber d. physiol. Dosirung von Digitalispräparaten. *Ther. d. Grgenw.* n. s., Vol. 4, p. 112. 1902. Klemperer, *Ther. d. Gegenw.* n. s., Vol. 6, p. 526. 1904. Wendt, G. Doctor und Apotheker, im dunkeln Spiegel galenischer Präparate. *Med. Woche.*, Vol. 6, p. 100. 1905.

[2] Edmunds, C. W. Standardization of Cardiac Remedies. *Jour. Amer. Med. Assoc.*, Vol. 48, p. 1747. 1907.

[3] Assisted by T. C. Ladakis, Ralph R. Johnston, Edgar R. Buzzell, D. H. Reighter, and S. T. Bonnell.

Primarily, it should be said that in the opinion of the writers there are too many formulas for elixirs contained in this book, which is now a standard Formulary for the United States, there being eighty-eight formulas in all.

For instance there are five formulas for bromides; *i. e.*, simple solutions of the individual bromide in a sufficient amount of aromatic elixir. In the first place the, 23 or 25 per cent. of alcohol present is directly antagonistic to the effect of the sedative; and secondly, why should a simple formula of this character be given when a physician could far better select his own dose of bromide or medicament and the vehicle which he desires to carry it?

This latter criticism may be applied to the following elixirs, although the several formulas, from a pharmaceutical standpoint, are satisfactory:

Elixir of ammonium bromide, calcium bromide, lithium bromide, lithium citrate, lithium salicylate, potassium acetate, potassium bromide, sodium bromide, sodium hypophosphite, and sodium salicylate, while the list might be further extended.

There is no criticism to be made upon the following additional formulas; they are pharmaceutically satisfactory:

Elixir of ammonium valerianate (the title should be "valerate"); ammonium valerianate and quinine; bismuth; buchu; compound buchu; compound cathartic; compound chloroform; cinchona and iron; cinchona, iron, bismuth and strychnine; cinchona, iron and bismuth; cinchona, iron and calcium lactophosphate; cinchona, iron and strychnine; coca and guarana; compound digestive; eucalyptus; iron pyrophosphate; iron hypophosphite; iron phosphate; gentian; gentian and iron chloride; gentian and iron phosphate; glycyrrhiza; guarana; hypophosphites; pepsin; pepsin and bismuth; compound tar; pilocarpus; potassium acetate; hops; pepsin and iron; quinine valerianate (valerate); rhubarb; strychnine valerianate (valerate).

The following criticisms are offered with the hope that they may call attention to difficulties, and, if the elixir is retained in the next edition of the National Formulary, may be made more satisfactory:

ELIXIRS.

Salicylic Acid.—The salicylic acid dissolves very slowly and with great difficulty. It contains 50 per cent. of glycerin and is really a

glycerite. Even a larger amount of glycerin, however, would aid solution.

Anise.—The formula is very unsatisfactory. The odor is not that of anise, but strongly of bitter almond, and considerable oil separates, making an unsightly preparation. While the separation of oil is recognized by the "Note" in the N.F., there can be no reason for the excess.

Caffeine.—It was entirely impossible to dissolve the caffeine in the 125 c.c. of aromatic elixir directed. Experiments show that 625 c.c. is sufficient and a change should be made in the directions.

Calcium Hypophosphite.—The salt dissolves very slowly, a small portion remaining undissolved. It is doubtless the fault of the salt, yet it seems to be impossible to buy an article which is wholly soluble. One worker has suggested the solution of a freshly precipitated salt to avoid the difficulty.

Calcium Lactophosphate.—The directions are faulty. When the calcium lactate was rubbed with the phosphoric acid, water and syrup, it would not dissolve; but when first dissolved in the phosphoric acid and then mixed with the other ingredients, no difficulty was encountered.

Compound Cathartic.—Considerable sediment separates from this elixir after standing a few weeks. This criticism applies to most of the elixirs made from fluidextracts, including: coca, aromatic eriodictyon, euonymus, frangula, grindelia, cascara sagrada, and compound taraxacum.

Cinchona.—In this era of correct titles, this elixir can hardly be called "cinchona," since it is made from cinchona alkaloids and artificially colored. The preparation is very satisfactory from a pharmaceutical standpoint.

Cinchona and Hypophosphites.—The hypophosphites, at least the calcium hypophosphite, dissolved with great difficulty. The color is considerably lighter than the "elixir of cinchona." The acid may be responsible for this color change.

Cinchona, Iron and Pepsin.—This preparation develops a slight white precipitate, as do also the several other elixirs containing pepsin, *i. e.*, cinchona, pepsin and strychnine; plain pepsin; pepsin, bismuth and strychnine; pepsin and bismuth; pepsin and iron.

Coca.—After a few days the elixir became cloudy, talc was added and the preparation again filtered. The elixir has again become cloudy.

Curaçao.—It has been impossible to buy oil of curaçao orange from available sources, from which to make the spirit and subsequently this elixir.

One of the large volatile oil manufacturers has submitted the following letter when asked to explain what was formerly sold as oil of curacao orange:

"Replying to your inquiry of the 6th inst., we fear that you are chasing a rainbow. Curaçao oil of orange undoubtedly is to-day, and in our opinion always has been, a fiction, at least in so far as its position as a commercial article is concerned. The oil that was formerly brought here under this name was probably nothing more than regular bitter orange oil, or possibly a blend of bitter and sweet orange toned up with other aromatics to give it character."

Prof. C. Lewis Diehl, Chairman of the Committee on National Formulary, in reply to this letter, has stated that this formula was included in the original New York and Brooklyn Formulary, out of which grew the N.F., and that probably at that time there was a genuine oil of curacao orange, and if not, the men of that time (1888) were using the best information available.

He states that he has often discussed the subject and advocated many years ago that an oil of bitter orange be introduced for the present oil of curacao in the N.F.

Lactate of Iron.—It was found that by dissolving the potassium acetate first in the water and then the lactate of iron, solution was greatly facilitated.

Pyrophosphate of Iron, Quinine and Strychnine.—The addition of talc before filtering improves the appearance of the elixir.

Iron, Quinine and Strychnine.—This formula is satisfactory, if the tincture of citro-chloride of iron has been made in accordance with the latest issues of the N.F., third edition. The first printing of the third edition called for 410 grammes of sodium citrate. This was shown to be unsatisfactory, and it has been increased in books more recently printed to 425 grammes.

Glycerinated Gentian.—This elixir has been repeatedly criticised for the presence of both acetic ether and solution of saccharin. The formula needs revision.

Aromatic Glycyrrhiza.—This preparation is somewhat turbid; the presence of both a fluidextract and volatile oils may account for this. It is not very satisfactory pharmaceutically.

Glycerophosphates.—Several different makes of the glycerophosphates have proven unsatisfactory. Mr. Dunning has stated that acid glycerophosphate of calcium is the salt required in this formula. A few drops of phosphoric acid will dissolve the precipitate. Solution was obtained in all cases; but upon standing, a voluminous white precipitate developed.

Hypophosphites with Iron.—The elixir has deposited a slight precipitate.

Lithium Salicylate, and other salicylates.—For a colorless preparation of these salts it is essential that a colorless and high-grade chemical be obtained. When bought on the open market, such a lithium salicylate was not received, and consequently the preparation is badly discolored.

Malt and Iron.—The wholesale houses on several occasions have reported that they are unable to supply extract of malt U.S.P. for making this preparation.

Paraldehyde.—This elixir separates into two distinct layers, the top layer occupying about one-fourth of the volume. It has become discolored upon standing two months. It has been suggested that if the alcohol be increased, this separation will not occur. It now contains over 50 per cent. of alcohol, however, and is given in a two fluiddrachm dose, so that its uses, especially if the alcohol is yet further increased, are questionable.

Phosphorus.—This was a U.S.P. 1890 preparation and the formula should be in the Appendix. The only change in the formula is that of directing 560 c.c. of glycerin, the U.S.P. 1890 ordering 550 c.c.

Potassium Acetate and Juniper.—A slight deposit forms upon standing.

Compound Quinine and Phosphates.—Although a solution was first obtained, a voluminous precipitate soon formed. This elixir should be further experimented with, if the preparation is to be retained.

Compound Blackberry.—As blackberries were not in season and the fresh juice was unobtainable, this elixir could not be made.

Elixir Terpin Hydrate.

Elixir Terpin Hydrate with Codeine.

Elixir Terpin Hydrate with Heroine.

In all of these elixirs a heavy crystalline precipitate has formed. It was first supposed to be terpin hydrate; but as its volume soon exceeded the amount of that substance in solution, it was suspected

to be sugar, and a simple investigation of this precipitate proved such to be the case. The crystals were entirely soluble in a small quantity of water, and were sweet to the taste, forming a syrupy-like solution. The elixir contains about 40 per cent. of alcohol, which is necessary for the solution of the terpin hydrate. Doubtless the amount of syrup will have to be reduced.

Of the eighty-eight elixirs of the N.F., the following eleven have not been prepared; all of the others are displayed:

Elixir of hops; phosphorus; phosphorus and nux vomica; compound cascara sagrada; rhubarb and magnesium acetate; compound stillingia; turnera; compound viburnum opulus; viburnum prunifolium; malt and iron; and zinc valerianate (valerate).

IMPROVED ACETONE CANTHARIDAL COLLODION.

By George M. Beringer.

The active principle in cantharides is present partly in a free or uncombined state and partly as a salt in combination with the natural acid as cantharidate. The cantharidate is insoluble in chloroform and ether, and most of the ordinary solvents in which cantharidin is soluble, and which are used in making the pharmaceutical preparations.

Analyses published by N. Dietrich [1] and Boudin [2] show that the combined cantharidin amounts to from 10 to 20 per cent. of the active constituent of the beetle.

In the official process for cantharidal collodion the powdered drug is percolated with chloroform and so only the free cantharidin is extracted and varying proportions of the drug activity is discarded with the marc.

As long ago as 1852, Prof. Wm. Procter, Jr.,[3] pointed out that acetone was an excellent solvent for cantharidin and this has since been confirmed by a number of investigators. Schmidt [4] gives the solubility of cantharidin in acetone as 1 in 38, in chloroform 1 in 66,

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[1] *Pharm. Centralh.*, 42,674, Year Book of Pharmacy, 1902, p. 169.
[2] *Journ. de Pharm. et de Chémie*, 1888—18,391.
[3] Amer. Jour. of Pharmacy, 1889, p. 264.
[4] *Pharmaceutische Chemie*, 9—1874.

and the British Pharmaceutical Codex[1] states its solubility in acetone as 1 in 40, in chloroform 1 in 65, in acetic ether 1 in 150, in ether 1 in 700, and still more sparingly in alcohol. Many of the statements of the authorities concerning the solubility of this principle are, however, discordant and the subject is in need of further critical study.

The writer[2] has elsewhere called attention to the peculiar and valuable solvent properties of acetone and its remarkable miscibility with other solvents as well as with water. Since that time it has been officially recognized and directed in the preparation of some of the oleoresins and its application in numerous manufactures has made it an article of considerable commercial importance, and supplies of pure acetone, suitable for pharmaceutical purposes, are now available at moderate prices.

More recently[3] he proposed its use as a substitute for ether in the preparation of collodions. In the latter communication a formula was given for an acetone cantharidal collodion, and the object of this note is to publish the results of more recent study and submit the following improved formula:

ACETONE CANTHARIDAL COLLODION.

Take of Cantharides in fine powder	60 grammes
Glacial acetic acid	5 c.c.
Pyroxylin	4 grammes
Camphor	1 gramme
Acetone sufficient quantity to make	100 grammes

Mix the glacial acetic acid with 55. c.c. of acetone and moisten the powdered cantharides with this mixture and set it aside in a closely covered container for twenty-four hours. Then pack in a cylindrical percolator and slowly displace with acetone until exhausted. Reduce the percolate by distillation on a water-bath to 95 grammes, and when cold dissolve in this the pyroxylin and camphor. If necessary, make up weight with acetone to 100 grammes.

If the rate of percolation is rapid, from 125 to 150 grammes of percolate will be obtained befor the drug is exhausted, but by carefully regulating the flow the cantharides will be practically exhausted when 95 grammes of percolate is secured.

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[1] *Br. Ph. C.*, 204.

[2] AMER. JOUR. OF PHARMACY, 1892, p. 146.

[3] Proceedings A. Ph. A., 1906, p. 502.

In this formula the glacial acetic acid liberates the combined cantharidin and the resulting preparation represents the full activity of the drug. The finished product is clear, green in color, and exceedingly active. It is a marked improvement over the present official cantharidal collodion and should displace that formula in subsequent revisions.

THE PHARMACOPŒIA OF SWITZERLAND.

By M. I. Wilbert,
Apothecary at the German Hospital, Philadelphia.

"Pharmacopœia Helvetica, Editio Quarta," is the official title of the book, that, in many respects at least, appears to embody the most recent researches and the most modern advances in matters pharmacopœial.

This new fourth edition of the Swiss Pharmacopœia became the official standard for medicinal substances throughout Switzerland, on March 1, 1908, and, largely on account of its comprehensiveness and scientific character, the book itself has attracted an unusual amount of attention in pharmaceutical circles abroad.

Even the most cursory inspection of the Swiss Pharmacopœia will convince the trained pharmacist that it is a book that contains much that is original and evidences great thoroughness in its preparation. Every page of this book is so indicative of painstaking, conscientious work on the part of the members of the revision commission, that it would be difficult indeed to single out any one department or portion of the book as being even suggestive of greater thoroughness than any other.

Throughout the book there are indications that the individual apothecary of Switzerland must be a man of considerable training and attainment, and one who has developed the science as well as the art of his calling to a high degree. The need for testing all available medicaments for their identity, and, so far as possible, for their quality and purity, is everywhere emphasized, and considerable care appears to have been exercised in the selection of tests and processes for applying them, so as to provide methods that can be followed with a minimum of time and material. Care has also been exercised to restrict tests and methods within reasonable limitations, and everywhere the resources and the limitations of the ordinary

apothecary shop have been considered. Thus the revision commission thought it wise to omit all polarization and refractometer tests, as it was thought inexpedient to compel the average pharmacist to equip himself with the necessary, usually expensive, apparatus. The permissible variations of these several factors have, however, been added in a table, as an appendix, for the information and guidance of such dealers, chemists and others who may be equipped with the apparatus necessary to make the various determinations or tests.

The detailed classification of crystals has also been omitted for the reason that pharmacists do not usually have access to a goniometer, and the commercially obtainable crystals are seldom or never perfectly developed.

The history of the Swiss Pharmacopœia is particularly interesting in that it was originated and developed by pharmacists. The first of the distinctly national pharmacopœias of Switzerland was published in 1865 as a private enterprise of the Swiss Society of Apothecaries. This first edition of the Swiss Pharmacopœia appears to have been little more than a formulary, and was followed in 1872 by a second edition, also elaborated and published by the Society of Apothecaries. This book contained, in addition to formulas, descriptions of simples and crude drugs.

The second revision of the Swiss Pharmacopœia was begun by a committee of five members, appointed by the Swiss Society of Apothecaries in 1884, and was subsequently completed by an official Pharmacopœial Commission appointed in 1888.

This Commission consisted of twelve apothecaries, eight physicians, nine chemists and two veterinarians, who completed their work in 1893. The resulting pharmacopœia was printed in the three official languages, German, French and Italian, and became the official standard in all of the several Cantons but one—Glarus.

The present, fourth, edition of the Swiss Pharmacopœia has been revised by the members of the now existing official Swiss Pharmacopœial Commission, comprising two divisions, medical and pharmaceutical, subdivided into nine committees, each presided over by a chairman directly responsible for the accuracy of the work done by his particular committee. This edition of the Swiss Pharmacopœia is particularly interesting in that it is the first to be generally recognized by all of the several Cantons.

The book comprises a total of 672 pages, 34 of which are devoted to the introductory chapters and 517 to the description of the 853 officially recognized articles. Compared with the previous third edition, we find that 151 articles have been added, while no less than 95 have been discontinued, leaving a net gain of 56.

Simple figures, however, give but an inadequate indication of the amount of work that was involved in the revision of this book, particularly in view of the fact that every monograph in the Pharmacopœia was rewritten and elaborated on for this particular edition.

The provisions of the International Conference for the Unification of Formulæ for Potent Medicaments have been included in their entirety, as a portion of the introductory chapter, and, in the body of the book, the names included in the protocol are invariably given as synonyms of the official title, followed by the designation (P. I.) Prescription or Protocol International.

The general adoption that has been accorded to the provisions of the Brussels Conference must be a matter of considerable satisfaction to the men who took part in that conference. Commencing with the Pharmacopœia of the United States, which, it has been estimated, complies with but 27 per cent. of the requirements, practically all of the other pharmacopœias published by countries represented in the Brussels Conference include the greater number, if not all, of the provisions recommended in the Protocol. The pharmacopœias so far published include the Spanish, Belgian, Dutch, Austrian, Danish and Swiss. The introductory chapter of the Swiss Pharmacopœia contains a rather interesting definition for medicines, as follows:

"Medicaments—medicinal substances are substances or mixtures that are used for the prevention or removal of abnormal conditions or processes in the human or animal organism, or for the amelioration of disturbing, disagreeable or dangerous manifestations."

This definition is then further elaborated into forms of medicines and their method of application or use.

A chapter on "General Directions" includes definitions for and descriptions of a number of terms, processes and methods not described in detail in connection with the several monographs in the book itself. Thus we find a general definition for what is meant by warm or hot water and by ordinary or medium temperature. We also find directions for the determination of the specific gravity,

melting point, boiling point, solubility and ash content of substances. Also detailed descriptions of maceration, percolation and sterilization.

Altogether, these general directions include twenty-eight headings and contribute much to the avoidance of unnecessary repetition of details in connection with the several monographs in the body of the book.

The descriptions of chemical substances are terse, direct and readily understood. All of the descriptions are systematically arranged, and include, as headings, the Latin title, followed by the official German, French and Italian titles. The descriptions themselves include an enumeration of the physical properties and a number of qualitative tests. These are followed by tests for purity, the limit of contamination and an enumeration of the minimum per cent. of chemically pure substance that is indicated by the compliance with the several tests.

Whenever necessary, this description is further augmented by directions for keeping and an enumeration of the maximum single and daily dose.

Wherever the composition or the physical properties of a chemical substance depend on the method of preparation, a formula and the directions for making the substance have also been included. Thus the Swiss Pharmacopœia contains formulæ and directions for the several subsalts of bismuth, many of the salts of mercury and also a number of the preparations of iron.

The recognition of patented articles presents difficulties that are not readily met in a satisfactory manner, and this new Swiss Pharmacopœia offers nothing new in this respect. All of the older synthetics, such as salol, phenacetin and sulphonal, are admitted under Latinized titles of the well-known trade names; the newer products, however, products that are still protected by patent or trade rights, have been included under their chemical names, with the trade names, as synonyms, enumerated in the index.

While such names as acidum acetylsalicylicum (Aspirin) and acidum diaethylbarbituricum (Veronal) may be practical, it is indeed doubtful if any appreciable number of medical men would take kindly to trimethylbenzoxypiperidinum hydrochloricum (Eucaine).

The descriptions of the crude drugs are collected and classified under the parts of plants represented, with the prefix itself restricted

to the singular. Thus we have flos, folium, semen and tuber. Considerable care has been exercised to differentiate the parts of plants more accurately, so that drugs consisting largely or entirely of rhizomes are classed as such and not as roots.

The descriptions of crude drugs are, as a rule, exhaustive, and include not alone a minute description of the botanical characteristics, but frequently also chemical tests and microscopic details.

The title of the more important, or potent drugs is followed by the international titles as synonyms, and then the official German, French and Italian titles, in the order given.

The monographs usually include an enumeration of the source or origin of the drug, the botanical description, a microscopical description and an enumeration of the cells or cell contents that are indicative of adulteration, chemical tests for identity, assay process when adopted, the limit of ash content, and an enumeration of the physical properties, such as taste and smell. With many drugs this description is further augmented by directions for keeping, an enumeration of the maximum daily and single dose, and this in turn is followed by a list of the official preparations that are made from the drug.

Assay processes have been included for such drugs as: Aconite, belladonna leaf, belladonna root, cantharides, cinchona, coca, hyoscyamus, hydrastis, guarana, ipecac, gelsemium, kola, nux vomica, sabadilla, stramonium and veratrum.

For a number of other drugs, such as aloes, frangula, digitalis and strophanthus, qualitative chemical tests have been included. The drugs of animal origin have been augmented by vaccine virus, a general description of serums, and specific descriptions of antidiphtheritic and antitetanic serums. The glandular structures of the animal organism, and the many derivatives that have been introduced do not appear to have been thought of sufficient importance to warrant their being included at this time.

The formula and directions for the several galenical preparations, particularly the liquid preparations, are usually augmented by briefly stated standards for color, taste, density and general appearance. Not infrequently qualitative and at times quantitative chemical tests serve to further complete the description.

The general scarcity of complex galenical preparations is one of the features that must be particularly gratifying to the scientifically

educated pharmacist or physician in that it is indicative of scientific rather than slipshod training on the part of medical practitioners.

The large number of general headings, or directions for making certain classes of preparations, readily makes up for the apparent lack of numbers in some of the different classes.

The Pharmacopœia is further augmented by a series of twenty-three tables which serve as an elaboration of the several monographs.

Among the more interesting of these tables is a list of reagents for medical purposes. This includes formulæ for the tests and stains that are used in the examination of the several secretions and excretions, the examination of blood and the staining of micro-organisms. Then there are a number of tables that are of special interest to the student or the physician. For example, there is a list of articles that are to be kept apart from others, a list of the poisonous or potent articles, a table of maximum single and daily doses, and a table of the per cent. content of active ingredient in the several galenical preparations.

The table or list of atomic weights is, in accordance with the generally adopted practice in Europe, based on oxygen = 16.

An index and list of synonyms, covering fifty-two double column pages, serves as a ready reference to the material contained in the book.

Altogether it may be confidently expected that this new pharmacopœia will surely serve to retain for the Swiss pharmacist the respect of the medical profession in his own country, in that it will necessitate his continuing the practice of his calling along scientific lines, and thus secure for him recognition far outside the limits of his own country. The admiration and the praise that has been so generally expressed throughout Europe, for the scientific character and the practical value of the material presented in the Swiss Pharmacopœia is amply justified and the book itself is certainly well worth careful study and consideration on the part of all who are in any way interested in the elaboration or improvement of our own Pharmacopœia of the United States.

THE PHILADELPHIA BRANCH OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

The meeting of the Philadelphia Branch of the American Pharmaceutical Association, held on the evening of May 5, 1908, was devoted to a discussion of "Pharmaceutical Associations and Their Uses."

Mr. M. I. Wilbert read a paper on "The Status of Pharmacy and Pharmacists in Europe," in the course of which he reviewed some of the achievements of the earlier pharmacists abroad and outlined some of the aims and objects of pharmaceutical societies in the several countries of Europe. He asserted that, from a scientific point of view, it was unfortunate, indeed, that pharmaceutical as well as medical training and practice in the United States should be based on the antiquated and undeveloped system in vogue in Great Britain a century or more ago. The precedent thus established has severely handicapped the progress of the science of pharmacy in this country, and it will be many years before we can entirely eliminate the hampering influences of the old-time affiliations that, at times at least, appear to all but overshadow the true vocation of the pharmacist.

In concluding, he expressed the belief that the work that is being done in Europe, and even the work that is being done in connection with the American Medical Association, will be of but indifferent value to American Pharmacy unless pharmacists themselves are able and willing to assist, in a practical way, by perfecting themselves in the science of their calling and by insisting that future generations of pharmacists receive, and are able to profit by, a more complete and better form of pharmaceutical education than has been offered them heretofore.

Mr. Thomas H. Potts, the president of the National Association of Retail Druggists, presented a communication entitled, "The N.A.R.D. as a Factor in the Progress of Pharmacy."

After briefly outlining the conditions as they existed a decade or more ago, before the founding of the N.A.R.D., Mr. Potts recounted some of the benefits that have been secured by organization along business lines.

One of the fundamental principles of the N.A.R.D., he believes, has been to make the business of the retail druggist pay him better, and in this, he asserted, the N.A.R.D. has been eminently successful.

The N.A.R.D. was founded to safeguard and to advance, in every honorable way, the welfare of the retail druggist. Every druggist who is imbued with the spirit of craft kinship, and realizes the harmonizing power of co-operation, should be a member of this organization.

Prof. Joseph P. Remington, in commenting on the paper by Mr. Potts, said that at the present time retail druggists are virtually compelled to give much of their attention to the immediate need for securing bread and butter, and they have little or no time or inclination for following up the professional side of their calling.

He believes that the enactment of pure food and drug laws, and the accompanying acceptance of the Pharmacopœia and of the National Formulary as legal standards, will serve to arouse both the physician as well as the pharmacist to an appreciation of the opportunities now before them, and will serve to elevate the retail druggist to a much higher plane.

Prof. Henry Kraemer read a paper on: "The Reorganization of the American Pharmaceutical Association," in which he expressed himself as being in favor of the form of organization that has been adopted by the American Medical Association, with the local society as the unit in the general scheme of organization.

He believes that pharmacists, collectively or individually, can no longer lose sight of the scientific side of their calling. The methods as well as the work of the retail druggist will, in time, be open to the scrutiny of government officials, and it will not be long before the faults and the shortcomings to be found in pharmacy will be exposed and discussed.

Professor Kraemer believes that some provision should be made for post-graduate work by retail druggists who are interested in the science of their calling. He thinks that this work can best be introduced in connection with the meetings of the existing pharmaceutical associations, and for this purpose he is in favor of eliminating all of the regular business from the general sessions.

The several communications were further discussed by Messrs. Potts, Eppstein, Cliffe, Professor Remington and Professor Stanislaus.

The latter presented a series of resolutions, which were duly seconded, and, after some additional discussion, slightly amended and finally adopted as the expression of the members present, for the guidance of the executive committee for the coming year.

The resolutions, as finally adopted, are as follows:

Resolved, That the members of the Philadelphia Branch of the American Pharmaceutical Association recognize the importance of the work done by the N.A.R.D., and appreciate the need for retail druggists supporting the National Association of Retail Druggists in a practical way.

Resolved, That the members of the Philadelphia Branch of the American Pharmaceutical Association deprecate repeated changes in the by-laws of the American Pharmaceutical Association and favor the reorganization of this Association along broader and simpler lines, so as to provide for the transaction of all routine business by a widely representative elective body of delegates.

Resolved, That the members of the Philadelphia Branch of the American Pharmaceutical Association favor the suggestion that the several schools and colleges in this city be requested to give a series of lectures or demonstrations, in the nature of a post-graduate course of instruction, and that the executive committee of the local branch be requested to arrange, if practicable, for a series of demonstrations for such of the local pharmacists who may wish to attend.

Resolved, That the members of the Philadelphia Branch of the American Pharmaceutical Association reaffirm their endorsement of the work done by the Council on Pharmacy and Chemistry of the American Medical Association, and that individually they pledge their active support in favor of publicity and honesty in connection with medicines and medicinal preparations.

Resolved, That the members of the Philadelphia Branch of the American Pharmaceutical Association, recognizing the many shortcomings and the difficulties that beset a satisfactory revision of the National Formulary, pledge their active support and co-operation to the Committee on Revision of the National Formulary.

Resolved, That the members of the Philadelphia Branch of the American Pharmaceutical Association, during the coming year, take up and discuss "The Declaration on the Prescription" as promulgated by the Chicago Branch of the American Pharmaceutical Association.

M. I. WILBERT,
Secretary.

MAY PHARMACEUTICAL MEETING.

The last of the series of Pharmaceutical Meetings of the Philadelphia College of Pharmacy for 1907–8 was held Tuesday, May 19th, at 3 P.M. Among the visitors present was Mr. S. A. D. Sheppard, of Boston, the well-known treasurer of the American Pharmaceutical Association, who, upon invitation, acted as chairman of the meeting.

T. C. Ladakis, professor of pharmacy in the American College at Beirut, Syria, who has just graduated from the Philadelphia College of Pharmacy with the degree of Doctor in Pharmacy (P.D.), described the practice of pharmacy in Egypt.

Professor Ladakis said that, in considering the conditions of pharmacy in Egypt, it should be remembered that the country has been under English rule only since 1882. He said that the regulation requiring those who practice pharmacy in Egypt to be licensed pharmacists, dates back to 1888.

The Egyptian Government conducts a school of medicine and pharmacy at Cairo, which at the present time is well attended, for the reason that each graduate, whether of medicine or pharmacy, is assured a Government position. At first the instruction given in the school was in Arabic, but now it is in English, the professors being mostly Englishmen. The degree of Bachelor of Arts is required alike of the applicants for admission to the courses on pharmacy and on medicine.

Very few of the pharmacies in Egypt are conducted by natives, most of them being under the management of foreigners, including Englishmen, Greeks, Frenchmen, Italians, Germans, Syrians and others.

Professor Ladakis stated that the practice of pharmacy in Egypt is rendered more difficult by the two factors that the country has no pharmacopœia of its own, and the physicians, being also mostly foreigners, prescribe the preparations of their own pharmacopœias.

Under the pharmacy law adopted in 1904, the pharmacies of Egypt are regularly inspected, and samples of preparations analyzed at the Government chemical laboratory in Cairo, and when a preparation is found deficient, that is, not of the standard required by the pharmacopœia according to which it was prepared, the pharmacist is fined—for the first offense, fined and imprisoned; for the

second offense and for further offenses may have his store closed, or his permission to practice pharmacy revoked.

Graduates of practically all foreign schools or colleges of pharmacy are allowed to practice without examination.

Professor Ladakis said that pharmacists in the near East handle practically nothing but medicines, the only side lines being perfumery, toilet articles and photographic goods. He said that if pharmacists were to attempt to sell cigars, cigarettes, etc., the people would lose the respect which they have for pharmacists, and the present high position of the calling would be greatly lowered.

Proprietary preparations are used to some extent, and those manufactured in Egypt are either preparations for diseases of the eye or general tonics.

The practice of pharmacy in Turkey is about on the same plane as in Egypt, except that the professors in the medical and pharmaceutical schools regard the French pharmacopœia as the official guide.

In Turkey, certain chemicals, for one reason or another, are not allowed either to be manufactured or imported, and of these the following were mentioned: nitric acid, all nitrates (except silver nitrate) and chlorates, cocaine and its salts, sulphonal, potassium cyanide, picric acid, nitroglycerin, gun cotton, bismuth subsalicylate, cotton seed oil, and essence of cognac.

Other interesting points were also brought out in the discussion of the paper.

Mr. M. I. Wilbert gave an interesting résumé of some of the Recent Advances in Pharmacy (see p. 287), and exhibited and commented upon a line of pharmaceutical preparations which had been prepared by members of the local branch of the American Pharmaceutical Association for exhibition at the recent meeting of the American Therapeutic Society, held in Philadelphia.

Mr. Wilbert alluded to the spread of prohibition and local option, and said that pharmacists should take cognizance of the movement, as it is likely to cause a lessening of the amount of alcohol used in medicines and the employment of other means of preserving pharmaceutical preparations.

The speaker then enumerated a series of preparations which should be made by pharmacists, and in this connection spoke of the introduction of sterilization processes by European pharmacists.

He said that this is a subject to which the pharmacists of this country must give more attention in the future, it having been heretofore almost totally neglected.

The distinction between the terms "dispensing" and "compounding" in a legal sense having been announced for discussion, Mr. Wilbert said that while he was not familiar with the State law on this point, the rule seemed to be that wholesalers are allowed, without license, to compound or mix medicines so long as they do not dispense them, and thus it frequently happens that ignorant and uneducated assistants are employed in handling medicines. He said that Governor Pennypacker held that a wholesaler should not be allowed to compound medicines unless he had a pharmacist's license.

Prof. E. Fullerton Cook again called attention to the series of National Formulary fluidextracts and elixirs which were made under his direction by students during the College term, and said that he had received letters from manufacturers protesting against the adverse criticisms made on fluidextracts at the March Pharmaceutical meeting (see April number of this JOURNAL, p. 196), the claim being made that the use of fluidextracts is increasing. Professor Cook said that the increase in the use of fluidextracts is no doubt due to their use in other preparations, as tinctures, elixirs, wines, etc., and he pointed out the desirability of taking up and discussing the subject as to whether their use in this way is permissible.

Mr. Wilbert claimed that the method of dilution as recommended by some manufacturers on their fluidextract labels is not official, and should not be practiced. He wholly condemned the practice of making infusions from fluidextracts, and also said that tinctures should not be made by dilution of fluidextracts, because of the loss of active constituents through precipitation.

Dr. Clayton M. Thrush referred to a statement made by Dr. Janeway, of New York, that he found it very difficult to obtain the official tincture of digitalis. He said that he called the dilution method the "lazy method," and expressed the hope that it would soon cease to exist.

In reply to a question by Mr. C. P. Gabell as to whether, in the case of alkaloidal or standardized preparations, it would be better to make them by dilution of fluidextracts than from drugs of variable quality, Mr. Wilbert said that this subject had been discussed for

many years by Squibb, Rice and others, and that experiments showed that in the diluted fluidextracts, precipitation occurs and carries down the active ingredients.

Mr. Ambrose Hunsberger pointed out that certain manufacturers give the alkaloidal strength of powdered drugs.

A conjoint paper on "A Chemical and Microscopical Examination of Commercial Ginger," by Prof. Henry Kraemer and Mr. Harry E. Sindall, was presented in abstract (see p. 303).

Mr. Sindall stated that Circular 13, issued by the Government, permitted a yield of 8 per cent. of ash in ginger; but in Circular 19 the allowable percentage of ash was reduced to 6, which latter standard excludes Calcutta ginger. He stated that of eleven commercial samples which he examined, only one yielded less than 6 per cent. of ash, and this sample was found to be adulterated.

Professor Kraemer stated that he would not attempt a résumé of his work on ginger in the time at his command, but desired to refer to one or two points only.

Mr. Hunsberger presented to the College an old-fashioned brass hand prescription scale, and a spring lance formerly used by pharmacists as well as by physicians for bleeding their patients and for lancing ulcers.

J. N. Limbert & Co. exhibited a cutting of *Vanilla planifolia* recently received from Mexico, bearing a young green vanilla pod.

Dr. J. Henry Allen, of Savannah, Ga., presented a hand prescription balance used a century ago in the South. The balance is a fine one and has been carefully kept.

Professor Kraemer exhibited a specimen belonging to the College collection, which he said appeared to be very rare indeed, namely, a clustered or multiseriate ovulate cone of probably *Pinus rigida*. He said that he had become interested in the specimen through reading a recent article by Wieland, in the *American Journal of Science* (Vol. 25, page 102). Instead of the usual cluster of up to half a dozen cones, this compound cone consists of about fifty cones, and according to Wieland, there are only four other known specimens, viz., one found in the Silliman collection at Harvard University, and three in the *Jardin des Plantes*, Paris. These compound cones are considered to represent a primitive type, and are of interest more especially to the student of evolution.

FLORENCE YAPLE, *Secretary pro tem.*